Autism characteristics and behavioural disturbances in children with Down syndrome in England and Wales

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"I've always known my daughter is different to other children with Down's syndrome and used to think her behaviour and severe learning disability were down to the way I've brought her up. I'd be really interested to see what your research finds and to be able to share our experiences to help others."

Mother of a child with a confirmed diagnosis of
Down syndrome and co-morbid autism spectrum disorder

Abstract

Background: Despite initial beliefs that the association was very rare, recent research indicates that a substantial proportion of children with Down syndrome (DS) also meet diagnostic criteria for an autism spectrum disorder (ASD). Often it is the case that behavioural difficulties faced by these children are attributed to their existing diagnosis of DS and many parents experience major difficulties in obtaining an autism diagnostic assessment. In order to best advise families of children with the co-morbidity, a specific behavioural profile needs to be established.

Aims: (i) To ascertain how many children with DS in England and Wales screen positive for ASD (ii) To examine the behavioural phenotype of DS and co-morbid ASD (iii) To determine the impact of raising a child with DS and co-morbid ASD on the family.

Method: A questionnaire survey, conducted through the Down's Syndrome Association, screened 485 6-15 year old children with DS in England and Wales for autism characteristics and evaluated their emotional and behavioural profiles. From this sample, 50 children with DS (23 with ASD and 27 without) were assessed using adaptive behaviour, autism profile and challenging behaviour outcome measures. Fifty parents were assessed using stress, psychological morbidity and perceived support outcome measures. Thirty-five siblings were assessed using an emotional and behavioural outcome measure.

Results: The proportion of children with DS in England and Wales who screen positive for ASD is substantially higher than in the general population. However, these children show an atypical autism profile when compared with individuals with idiopathic ASD. These children also experience significantly greater behavioural problems than children with DS only and their parents report higher levels of stress than the parents of children with DS only.

Conclusions: Early detection of autism characteristics is important for appropriate intervention. However, the unusual autism profile of this group may affect the recognition of the disorder and hinder the implementation of appropriate interventions. Interventions that focus on challenging behaviours could help reduce difficulties for the children and stress in the parents.

Statement of originality

The project reported in this thesis was a combination of a questionnaire survey involving 1382 families and a group study involving 50 families. Funding for the study was obtained by my supervisor, Professor Patricia Howlin. The design of the study was undertaken jointly by me, my supervisors (Professor Patricia Howlin and Dr Patrick Smith) and Dr Joanna Moss.

Ethical approval for the questionnaire survey was obtained prior to my joining the project. Ethical approval for amendments to the questionnaire survey and for the group study was sought by me with input from my supervisors. Recruitment of the families was undertaken by me and the database administrator of the Down's Syndrome Association, Miss Ellie Walsh with support from my supervisors. The data were collected by me, with support from research assistants Ms Jennie Cox (for the survey) and Miss Kellyan Gayle (for the group study).

The thesis contains a comprehensive review and critical appraisal of the current research available in this field of study that is my original work, as is the detailed write-up of the methodologies. The hypotheses and research questions investigated and the variables that were selected for analysis were formulated by me. The data analyses conducted in the thesis were entirely my own work. All graphical presentation, interpretation, discussion and inferences drawn from these results are also based on my own thoughts and ideas. All written work, including a discussion of the findings, the critical appraisal of the study and suggestions regarding the implications of the findings and recommendations for future research, is entirely my own.

Acknowledgements

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My final thanks must go to the children and families who took part in the project. Research of this kind is only possible because of those who benevolently share their experiences to help others. I hope the dissemination of the research findings goes some way towards improving the understanding of the needs of these families and alleviating the difficulties that a number of them face in accessing appropriate help and support.

Publication

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PART A: INTRODUCTION AND LITERATURE REVIEW

Chapter 1: Introduction to Down syndrome

Outline

This introductory chapter provides a brief overview of the history, core characteristics, epidemiology, aetiology and common co-morbidities of Down syndrome.

1.1 History of Down syndrome

Past evidence of Down syndrome (DS) can be inferred by artistic depictions of the distinctive craniofacial features associated with the syndrome. A Neolithic representation of the condition in the form of a clay model indicates that DS is actually over 7000 years old (Diamandopoulos, Rakatsanis, & Diamandopoulos, 1997) and individuals with apparent DS can be found in artwork dating back to the sixteenth century (Levitas & Reid, 2003). However, DS was not discussed in scientific literature until 1866 when John Langdon Down and Edouard Seguin each published work on the condition (Down, 1866; Seguin, 1866). These works noted the unique physicality of individuals with DS. Regrettably, a racial perspective was adopted at this time and the syndrome was termed 'Mongolism', as epicanthal folds in the corner of the eye were common in both DS and the Mongolian race (Fidler & Daunhauner, 2011).

Research at the beginning of the twentieth century became focussed on discovering the aetiology of the syndrome. Maternal tuberculosis during pregnancy and thyroid dysfunction were among the incorrect theories put forward by academics (Clark, 1933; Muir, 1903). Yet, early research did identify mother's age as a critical determining factor, with recognition that the probability of the birth of a child with DS rises rapidly after the maternal age of 35 (Penrose, 1933; 1934). The production of more powerful microscopes in the 1950s led to the discovery of chromosomal abnormalities in the DS karyotype and the presence of additional chromosome 21 material was detected in 1958 (Lejeune, Turpin, & Gautier, 1958). Within a few years of this finding it was realised that DS can be caused by mosaicism whereby extra chromosome 21 material is only present in some cells or by the translocation of the additional genetic matter onto other chromosomes (Clarke, Edwards, & Smallpeice, 1961; Polani et al., 1960).

1.2 Core characteristics of Down syndrome

Section 1.2.1 Physical characteristics and health

There are a number of physical traits that can be used as an indication of DS and it was through the detection of these traits that DS was initially recognised (Down, 1866). The list is now extensive, with hundreds of characteristics having been identified; however, common features include epicanthic folds, up-slanted palpebral fissures (where the outer corner of the eye is turned up rather than down), Brushfield spots, a flat facial profile, a protuberant tongue, a single palmar crease and hypotonia, where muscle tone is low (Fidler & Daunhauer, 2011) (see Figure 1.1 for examples).

There is a well known association between DS and congenital heart defects, with incidence being reported at 44.2% (Freeman et al., 2008). The risk of other health concerns, such as hearing and visual impairments, is also raised in comparison to individuals with other forms of intellectual disability (Bull, 2011); these impairments can often be attributed to abnormalities in the form and structure of the ear, nose and throat commonly found in DS (Mitchell, Call, & Kelly, 2003). Early onset dementia, most commonly Alzheimer disease, has been well documented in DS (Holland et al., 2000; Tyrrell et al., 2001) and recent research indicates an earlier menopause in women with DS (Coppus et al., 2010). The two may be related and could indicate an accelerated aging process in people with DS.

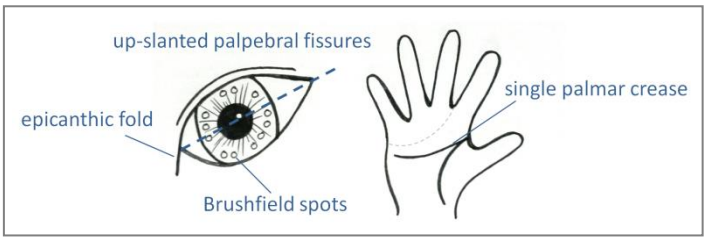

Figure 1.1 Examples of physical traits indicative of DS

Section 1.2.2 Behavioural phenotype

Cognition

Most individuals with DS fall into the mild to moderate range of intellectual disability, with intelligence quotients (IQs) ranging from 40 to 70 (Hodapp, 1999). In particular, individuals with DS have demonstrated difficulty with verbal short term memory tasks (Vicari & Carlesimo, 2006); these deficits do not appear to extend to long term memory for verbal information (Jarrold, Baddeley, & Phillips, 2007). Despite a comparative weakness

in this area, the short term memory skills of children with DS develop, along with general cognitive development, at a similar rate to typically developing children (Carney et al., 2013). It has been reported that, among children with DS, girls perform better than boys on short term memory tasks (Rihtman et al., 2010). Problems with motor planning are also common and reaction times and movement times tend to be slower for people with DS (Mon-Williams et al., 2001). Motor skills in general appear to improve later in childhood, and fine motor skills (e.g. copying, free writing and handwriting) also tend to improve over time (Rihtman et al., 2010).

Language

While there is individual variation, many individuals with DS show a disparity in language skills with expression being more impaired than receptive language; particular weaknesses include phonology and syntax (Martin et al., 2009). These difficulties in expressive language are more pronounced than would be expected based on cognitive functioning (Fidler, 2005). Although research into the area is scarce, hearing difficulties commonly experienced by individuals with DS may be related to receptive language skills; around 75% of children with DS have been reported to have hearing impairment (Bull, 2011). It has also been proposed that the facial physical traits associated with DS (see Section 1.2.1) may be linked to speech production resulting in subsequent impairments in phonology (Martin et al., 2009). However, phonological awareness programs have proven effective (Cleave, Bird, & Bourassa, 2011), suggesting that the cognitive weaknesses faced by individuals with DS are a more likely cause. Indeed, a strong link has been reported between phonological memory and expressive language skills in DS (Laws, 2004).

Social development

Social functioning is considered a relative strength in the DS behavioural phenotype (Fidler & Nade, 2007). Children with DS display higher levels of prosocial behaviour than children with other forms of developmental delay (Fidler, Barrett, & Most, 2005). They also show more empathy for others' emotions. For example, in a simulated distress situation, children with DS were found to offer reassuring responses, such as touching or patting, to a far greater degree than other children (Kasari, Freeman, & Bass, 2003). However, the play skills of children with DS are less advanced than both those of chronological-age matched peers and those of children matched for mental age. Children with DS are less involved in sustained group play and tend to play with established friends to a greater degree, rather than with new children (Guralnick, Connor, & Johnson, 2011).

Despite this, the play skills of children with DS are still considered relatively good and the prosocial behaviours that they display are believed to compensate greatly for the potential risk factors relating to their cognitive and language deficits (Guralnick et al., 2011). Nevertheless, although this is the case for young children, there is evidence that as individuals with DS get older they smile less, seek less social attention, become more anxious, withdrawn and depressed and generally experience greater levels of social problems (Fidler et al., 2005).

1.3 Epidemiology of Down syndrome

The population prevalence of people with DS in England and Wales in 2011 was estimated at 0.66 per 1000 people (Wu & Morris, 2013). An analysis of DS prevalence trends over a twenty year period highlighted a decline in the 1990s which was most likely due to the increased uptake in serum screening during this period (Irving et al., 2008). The proportion of women who decide to terminate the pregnancy when they receive an antenatal diagnosis of DS has remained constantly high at over 90% (Morris & Alberman, 2009). Furthermore, a high rate of miscarriage occurs in DS pregnancies, with the overall rate of spontaneous loss reported at 35% (Hook et al., 1995).

1.4 Aetiology of Down syndrome

For approximately 95% of individuals with DS additional chromosome 21 material is produced through non-disjunction (where chromosomes fail to segregate properly during meiosis) (Freeman et al., 2007). This is called Trisomy 21 and the vast majority of cases have a maternal origin (although a paternal origin is possible). It is likely that the observed risk related to maternal age is linked to this process. There are two other aetiological mechanisms that account for the final 5% of cases of DS (Freeman et al., 2007). Mosaicism can occur whereby chromosomal separation fails *after* fertilisation (during mitosis). Two cell lines are created; one has the standard amount of chromosomes and the other has additional chromosome 21 material. Translocation can also occur where genetic material from chromosome 21 is located on another chromosome. This can lead directly to the symptoms of DS, or a 'balanced' translocation can take place where there has been no overexpression of chromosome 21. However, if an individual with balanced translocation reproduces, an overexpression of chromosome 21 is likely to occur and the offspring will

have DS. Translocation DS cases tend to be more common in younger mothers (Jyothy et al., 2002).

The pathway from the overexpression of chromosome 21 to the observed phenotype of DS is not fully understood. Genes on the Hsa21 have been identified as a possible critical region. More specifically it is argued that the miRNAs produced by the extra Hsa21 genes cause a decreased amount of target proteins, which leads to features of DS. Increased amounts of such miRNAs have been found in hippocampus and heart samples of individuals with DS (Kuhn et al., 2008).

1.5 Co-morbidity in Down syndrome

Aside from the medical problems associated with DS (see Section 1.2.1), research on the co-morbidity of DS and other disorders has been limited. Behavioural disturbance in people with DS was previously attributed to the associated cognitive impairment and further diagnostic consideration or evaluation was rarely pursued (Capone et al., 2006). However, Ekstein et al. (2011) suggest that children with DS are at increased risk for Attention Deficit Hyperactivity Disorder, with prevalence estimated at over 40%. Mood disorders, including depression, have also been reported as common, and have been associated with obstructive sleep apnea syndrome (Capone et al., 2013). Furthermore, a number of studies have investigated the prevalence of ASD in DS (see Chapter 3).

Chapter 2: Introduction to autism spectrum disorder

Outline

This introductory chapter provides a brief overview of the history, core characteristics, epidemiology, aetiology and common co-morbidities of autism spectrum disorder. A comparison is made between autism spectrum disorder and Down syndrome.

2.1 History of autism spectrum disorder

Autism was first clinically defined around 70 years ago by Leo Kanner. He spoke of a unique syndrome that was characterised by abnormal speech and repetitive behaviours with an "anxiously obsessive desire for the maintenance of sameness" (Kanner, 1943). His comments were based on the observation of 11 children who shared these characteristics. The following year a further academic paper was published by Asperger (1944), who summarised the features of a similar group of children. Although alike in terms of behaviour, a fundamental difference between the two groups was the academic ability of Asperger's children; he reported great ability in maths and science and spoke of the 4 children he observed as "scientists" (Asperger, 1944, p.72).

Not only was there variability between the two groups of children but both Kanner and Asperger noted inconsistencies within the groups. Wing and Gould (1979) later proposed that what was being described in the early work was a "continuum of severity" (Wing & Gould, 1979, p.26). This is now a widely recognised concept and autistic disorder is characterised as a 'spectrum', which includes autism, autism spectrum disorder (ASD), Asperger syndrome and childhood disintegrative disorder (CDD). A 'sub-threshold' category of atypical autism or pervasive developmental disorder - not otherwise specified (PDD-NOS) also exists.

2.2 Core characteristics of autism spectrum disorder

Section 2.2.1 Definition of autism spectrum disorder

Until very recently autism was described as being characterised by a 'triad of impairments'. This stems from the proposal by Wing and Gould (1979) of three key features necessary to diagnose ASD; (i) impairments in social interactions, (ii) repetitive stereotyped behaviours, and (iii) a delay in, or complete lack of, language (Wing & Gould, 1979).

The most widely recognised criteria for ASD are currently provided in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (2013). The specific criteria are outlined in Table 2.1. The triad of impairments previously recognised by DSM-IV has been reduced to two domains under the single category of ASD. There is a lesser focus on language delays as these are neither universal nor unique to ASD. Asperger syndrome, PDD-NOS and CDD are all included under the title of ASD; Rett disorder has been removed from the manual entirely. Impairments must be present before the age of 3 years; although it is recognised that these impairments may not be identified until later. It has been reported that the average age of diagnosis is around 5 years (Mandell et al., 2010); however, there is a growing body of research into early indicators of ASD (e.g. Jones & Klin, 2013). Severity levels have also been introduced to the diagnostic procedure (see Table 2.2).

Qualitative impairment in social interaction

Marked impairment in non-verbal behaviours is common in ASD. Children with ASD are less likely to point, show objects, or use eye gaze to communicate. This is not to say that they are unable to use non-verbal communication. However, the quality of their behaviours is likely to be poorer; for instance, they are much more likely to directly manipulate an adult's hand (Stone et al., 1997). There is little shared enjoyment in ASD, and the frequencies of having friendships, peer relationships, and participating in social and recreational activities are all low in adolescents and adults with ASD (Orsmond, Krauss, & Seltzer, 2004).

Restrictive, repetitive and stereotyped patterns of behaviour

Restricted, repetitive and stereotyped behaviours common to ASD range from repetitive body movement, such as rocking and hand flapping, to more cognitively mediated symptoms such as intense interests or rituals. These behaviours can be socially inappropriate and if prevented or interrupted can cause high levels of anxiety and disruptive behaviour (Gordon, 2000). The patterns of these behaviours can change across the lifespan, with the behaviours generally being less frequent and less severe among older individuals than among younger individuals (Esbensen et al., 2009).

Table 2.1 DSM-V diagnostic criteria for ASD

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive; see text):
    1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions or affect; to failure to initiate or respond to social interactions.
    2. Deficits in nonverbal communicative behaviours used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
    3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behaviour to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

        Specify current severity:

        Severity is based on social communication impairments and restricted, repetitive patterns of behaviour

B. Restricted, repetitive patterns of behaviour, interests or activities, as manifested by at least two of the following, currently or by history, (examples are illustrative, not exhaustive; see text)
    1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g. simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
    2. Insistence on sameness, inflexible adherence to routines, or ritualised patterns of verbal or nonverbal behaviour (e.g. extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals need to take same route or eat same food every day).
    3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g. strong attachment to or preoccupation with unusual objects, excessively circumscribed or preservative interests).
    4. Hyper- or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment (e.g. apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

        Specify current severity:

        Severity is based on social communication impairments and restricted, repetitive patterns of behaviour

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies later in life).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

Table 2.2 DSM-V severity levels for ASD

Severity level	**Social communication**	**Restricted, repetitive behaviours**
Level 3 "Requiring very substantial support"	Severe deficits in verbal and nonverbal social communication skills cause severe impairment in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. For example, a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and responds to only very direct social approaches.	Inflexibility of behaviour, extreme difficulty coping with change, or other restricted / repetitive behaviours markedly interfere with functioning in all sphere. Great distress / difficulty changing focus or action.
Level 2 "Requiring substantial support"	Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal responses to social overtures from others. For example, a person who speaks simple sentences, whose interaction is limited to narrow special interests, and who has markedly odd nonverbal communication.	Inflexibility of behaviour, difficulty coping with change, or other restricted / repetitive behaviours appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and / or difficulty changing focus or action.
Level 1 "Requiring support"	Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful responses to social overtures of others. May appear to have a decreased interest in social interactions. For example, a person who is able to speak in full sentences and engages in communication but whose to-and-fro conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful.	Inflexibility of behaviour causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organisation and planning hamper independence.

Section 2.2.2 Behavioural phenotype

Cognition

Approximately half of children with ASD have an intellectual disability (i.e. IQ<70) (Charman et al., 2011). Despite heterogeneity in ability, individuals with ASD appear to have a distinct cognitive profile, with relative strength in visual tasks and relative weakness in comprehension tasks (Charman et al., 2011). Children with ASD demonstrate poorer everyday memory (Jones et al., 2011) and episodic memory (Southwick et al., 2011) than typically developing children.

Language

Although the DSM-V focuses more generally on social-communication impairments, specific deficits in language expression and comprehension are common in ASD. The level of spoken language is variable; some children have a vocabulary, grammatical knowledge, and articulation skills within the normal range, while a substantial proportion remain essentially non-verbal (Groen et al., 2008). Those who are verbal may show stereotyped / repetitive use of language, idiosyncratic language and / or difficulties in initiating or maintaining conversation.

Sensory impairment

The DSM-V introduces sensory impairment as a core characteristic of ASD. Atypical sensory responses may manifest in different ways. Individuals with ASD may exhibit *hypo-responsiveness* where there is an apparent failure to register a sensory input. Conversely, they may exhibit *hyper-responsiveness* toward stimuli, which suggests a lower sensory threshold. For instance, they may be able to hear a distant noise before others. Many individuals with ASD engage in what is termed *sensory seeking,* whereby they engage in certain behaviours for the purpose of sensory feedback (Foss-Feig, Heacock, & Cascio, 2012). The different forms of sensory impairments are noted across the auditory, visual and somatosensory systems. (Tomchek & Dunn, 2007; Joseph et al., 2009).

2.3 Epidemiology of autism spectrum disorder

Early studies of ASD conducted in the 1960s indicated a prevalence of 4-5 per 10,000. The disorder was reported to be about four times more common in males than females. The characteristics of the children in the studies varied enormously. Prevalence estimates began to increase in the 1980s, with reports of above 10 per 10,000 (Fombonne, 2009). Today the

figure of 1 per 100 is typically used to indicate prevalence in the UK (Baird et al., 2006; Brugha et al., 2011).

Although there are few regional differences in the UK regarding the number of diagnoses, regional differences in the age at which an official diagnosis is obtained have been reported (Howlin & Moore, 1997). Later diagnoses are also more likely in children of less well-educated parents and there are differences found in the extent to which children of minority ethnic groups receive formal diagnoses of ASD (Rice et al., 2004).

The continued rise in prevalence estimates of ASD has attracted much attention. This could be a true prevalence increase, or a reflection of an increased awareness of the disorder. It is argued that a much narrower definition of autism was applied in the 1960s, thus excluding many cases that would be incorporated in the figure today (Fombonne, 2009). The recent changes to the clinical definition of ASD (see Section 2.2.1) may alter this trend; the reduction in the core diagnostic criteria in the DSM-V could lead to a change in the number of diagnosed cases, which could impact future prevalence studies.

2.4 Aetiology of autism spectrum disorder

As ASD is a heterogeneous syndrome, for which the diagnosis is based on behavioural characteristics, establishing aetiology is difficult. However, several causes have been put forward. Like many other psychiatric conditions, ASD appears to have a genetic component. Neurobiological correlates of the disorder are also generally accepted.

Section 2.4.1 Genetic factors in autism spectrum disorder

Family studies provide strong evidence for a genetic basis of ASD. Around 60% concordance of autism has been reported between monozygotic twins, and 20% in dizygotic twins (Hallmayer et al., 2011). Behaviours qualitatively similar to ASD (i.e. the Broader Autism Phenotype [BAP; Folstein & Rutter, 1977]) have been reported as more common in relatives of individuals with ASD than in the general public, and most commonly in families with several children with ASD (Losh et al., 2008). Family ASD recurrence rate is reported at approximately 10%, with an additional 20% of siblings experiencing language delay, many of whom exhibit ASD qualities of speech (Constantino et al., 2010). Advancing paternal age has been associated with an increased risk of ASD, although risk figures vary (e.g. Reichenberg et al. (2006): ASD 6 times more likely with father ≥40 rather than ≤30 years; Hultman et al. (2011): ASD 2 times more likely with father ≥50 rather than ≤30 years). Other studies suggest that maternal age is a determining

factor (Durkin et al., 2008; Grether et al., 2008). However, Shelton, Tancredi and Hertz-Picciotto (2010) identified interdependence between paternal and maternal ages when assessing the risk of ASD in offspring.

A recent review of research into the genetic aetiology of ASD (Talkowski, Minikel & Gusella, 2014) identified several ongoing lines of investigation. A recessive model of ASD suggests that 'loss of function' allele mutations (common to *all* individuals) occur in a chance combination affecting critical genes in individuals with ASD. However, this mode of inheritance is estimated to explain only approximately 5% of ASD cases. Inheritance of recessive 'loss of function' allele mutations common to both the mother and father (most likely due to a limited ancestral gene pool) has been identified as a possible cause. De novo mutations, which may not be inherited, have also been associated with ASD and linked to advancing paternal age. Sibling studies have indicated that the rate of de novo mutations does not vary between affected and unaffected siblings, but the nature of the mutation does (i.e. the genes affected and the role of those genes). There are also consistent reports of structural variations (where segments of DNA have been duplicated or deleted) in individuals with ASD. These abnormalities are referred to as copy number variants (CNVs). Initial CNV studies identified large genomic segments; however, more recent research has defined a critical region. Balanced chromosomal rearrangements have also been linked to ASD (i.e. the genetic structure is altered but there is no over- or under-representation of a gene). Recent cloning studies have identified several genes with possible 'breakpoints' which can lead to balanced rearrangements.

Section 2.4.2 Neurobiological aspects of autism spectrum disorder

It is generally accepted that individuals with ASD have differences in brain anatomy, connectivity and/or function. In a recent review of neuroimaging in autism, Ecker and Murphy (2014) note the well documented increase in brain volume that occurs in many infants with ASD. They report that primary regions have been identified and volumetric differences in these regions are associated with the presence of certain ASD behavioural characteristics (e.g. frontotemporal regions and amygdalae associated with socioemotional processing, and frontostratial system with repetitive and stereotypic behaviour). However, what is yet to be determined is whether the volumetric differences are in cortical thickness or cortical surface area. Ecker and Murphy (2014) outline neurologists' beliefs that each is determined by a different type of cell. Cortical thickness is established by neurons, whereas cortical surface area is established by non-neuronal cells that provide support and protection for neurons. Atypical brain connectivity (e.g. reduced white matter) is also

recognised in the neurobiology of ASD. Recent advances in this area have indicated reduced connectivity in grey matter (estimated by the length of horizontal connections that link brain regions within the cortical sheet) that correlate with ASD symptom severity (Ecker & Murphy, 2014).

Practical aspects of neuroimaging (e.g. resolution) have somewhat constrained findings; however, a recent development has been multivariate pattern classification (MVPC). This combines several neuroimaging methods (e.g. structural magnetic resonance imaging / diffusion tensor imaging / positron emission tomography) and has been reported to produce patterns that discriminate between subgroups of ASD. Although very promising for early detection of ASD, Ecker and Murphy (2014) question the applicability of MPVC to clinical settings, particularly the ability to distinguish between ASD and related disorders (e.g. social anxiety disorder and attention deficit hyperactivity disorder).

Section 2.4.3 Environmental hypotheses

A range of environmental theories has been proposed; however, these either lack strong evidence or have been robustly disproven. For instance, a controversial hypothesis is that certain vaccinations can lead to ASD, an example being the measles, mumps and rubella (MMR) vaccination (Wakefield et al., 1998). Yet, none of the arguments suggesting a connection between vaccines and ASD have been empirically proven (Lord, Kim, & Dimartino, 2011).

2.5 Co-morbidity in autism spectrum disorder

Until fairly recently there has been little systematic study of co-morbidities in ASD. This may be due to the non-specificity of the symptoms in the disorder. In addition, the communication difficulties of individuals with ASD may restrict self-reporting of additional problems (Simonoff et al., 2008). However, there is an emerging consensus that behaviours often found in people with ASD are, in fact, features of other disorders. Simonoff et al. (2008) reported that psychiatric disorders are common and frequently multiple in children with ASD; 70% of their cohort had at least one co-morbid disorder and 41% had two or more. High rates of ADHD, oppositional defiant disorder, anxiety and depression were all found (Simonoff et al., 2008). Further to this, over 80% of a sample of children with PDD-NOS were reported to have a co-morbid psychiatric disorder (de Bruin et al., 2007), as well as over 90% of a sample of children with Asperger disorder

(Mukaddes & Fateh, 2010). Disruptive behaviour and anxiety disorders were common across the cohorts.

Despite these figures, the identification of certain co-morbid disorders is complicated by overlap in symptoms. As Matson and Nebel-Schwalm (2007) have noted, some conditions can be more easily identified in the ASD population than others; depression, for example, can be diagnosed more confidently than obsessive compulsive disorder (OCD), as many features of OCD exist within core ASD symptomatology whereas those of depression do not (Matson & Nebel-Schwalm, 2007). Furthermore, the Diagnostic and Statistical Manual of Mental Disorders (DSM), which is often central to studies investigating co-morbidity, has been questioned as a valid classification system for the ASD population; a recent study found that the IQ and language ability of individuals with ASD affected the application of the criteria in the manual, indicating that modifications need to be made (Witwer & Lecavalier, 2010).

2.6 Autism spectrum disorder in genetic syndromes

An emerging literature reports an association between ASD or 'autistic-like behaviours' and syndromes with a known genetic cause, such as Tuberous Sclerosis Complex (TSC), Fragile X syndrome (FXS), Angelman syndrome and DS (see Table 2.3 for a summary of ASD prevalence estimates in genetic syndromes, and Chapter 3 for a literature review of DS and co-morbid ASD). These associations may have implications with regard to understanding the genetic pathways underlying ASD more broadly. However, Skuse (2007) suggests that the genetic syndromes associated with ASD are so vast and diverse that it will prove very difficult to reach specific conclusions regarding the gene loci of ASD. Abrahams and Geschwind (2008) propose that, although the associated genetic syndromes arise from different abnormalities, the effects downstream are common – which results in the presentation of ASD. Skuse (2007) suggests that the Intellectual Disability (ID) associated with many genetic syndromes simply increases the risk that ASD or 'autistic-like behaviours' will be revealed; the presence of a genetic syndrome may act as a 'risk marker' for ASD characteristics rather than play a causal role. This model of association is clearly important for the present study, as DS is the most common chromosomal cause of ID.

Recent studies indicate that the prevalence of ASD increases with the degree of ID in both TSC and FXS (e.g. Jeste et al., 2008; Loesch et al., 2007). However, in both genetic disorders ASD has also been identified in individuals with mild cognitive

impairments or IQ in the normal range (e.g. de Vries et al., 2007; Hagerman et al., 2005). de Vries et al. (2007) report that, across the IQ range, 48% of individuals with TSC present with ASD; whereas 17% of individuals with TSC *without* ID present with ASD. Similarly, Molloy et al. (2009) report an association between ID and the presence of ASD characteristics in DS, but state that the degree of ID alone cannot solely account for the raised prevalence of ASD in this group.

The association between ASD and ID is well established, however, estimates of the degree of association vary. The Centers for Disease Control and Prevention recently published that around 50-60% of individuals with ASD have at least mild ID (CDC, 2014), whereas LaMalfa et al. (2004) report that 70% of persons with ASD have ID. Considering the association in the other direction, reports indicate that between 4-40% of individuals with ID have ASD (see Matson & Shoemaker, 2009 for a review).With the vast majority of individuals with DS having an ID, it should not be surprising that ASD is common in this group. Nevertheless, the belief that DS is rarely associated with autism (Rutter & Hersov, 1985) is still common among many clinicians and has also influenced researchers' understanding of the comorbidity. Thus, research studies in this area tend to be based on the premise that ASD and DS should co-occur at or below the rate in the general population (i.e. it is expected that around 1% or less of individuals with DS will have ASD). However, this fails to take account of the much greater risk of ASD in individuals with ID more generally.

Table 2.3 Summary of ASD prevalence figures and associated degree of ID within syndrome groups (adapted[1] from Moss & Howlin, 2009)

Genetic syndrome	**Associated degree of ID**	**Estimated prevalence of autism spectrum disorder**
Fragile X syndrome	Moderate to severe	21-50%
Rett syndrome	Severe to profound	25-40% (classic), 97% (mild)
Tuberous Sclerosis Complex	Normal to profound	15-89%; 17% (normal IQ)
Phenylketonuria	Normal to severe	5%
CHARGE	Normal to severe	15-50%
Angelman syndrome	Severe to profound	50-80%

[1] Row on Down syndrome omitted because a more up-to-date review is presented in Chapter 3

2.7 Comparisons of autism spectrum disorder with Down syndrome

Comparisons of ASD with DS highlight some similarities, namely the adverse effect of the developmental disorders on communication and the increased likelihood of an intellectual disability. However, there are many differences between the disorders (see Table 2.4).

Table 2.4 Comparison of ASD with DS

	Down syndrome	**ASD**
Epidemiology	Less than 1 per 1000	1 per 100
Aetiology	Chromosome 21	Unknown
Diagnosis	At birth	Around 5 years
Physical features	Obvious common features	No common features
Prosocial behaviour	High levels	Low levels
Communication disturbance	Common	Common
Intellectual disability	Most	Around 50%

Facts based on information presented in Chapters 1 and 2 (see previous sections for references)

Chapter 3: Literature review of Down syndrome and co-morbid autism spectrum disorder

Outline

This chapter provides an overview of studies that have investigated the prevalence of autism spectrum disorder in Down syndrome, and studies that examine the behavioural phenotype of the co-morbidity; the limitations of the studies are discussed. The need for further research in this area and the contribution of the current study are put forward.

Search strategy

A literature search of the electronic database PsycINFO was conducted using the OvidSP interface on 12/02/14 for the period 1806 to January week 3 2014. The purpose of the search was to retrieve all previous research into Down syndrome (DS) and co-morbid autism spectrum disorder (ASD). The search terms and number of hits retrieved are listed in Table 3.1. One hundred and seventeen publications were identified by the search. Titles and abstracts were read for relevance. The initial retrieval included a repeat publication and publications that were not directly relevant to DS and co-morbid ASD; many were in relation to the separate disorders but had used each as a comparison group within a study. Sixteen of the publications were read in full and included in the review[2]. Relevant citations from these 16 publications were also followed up[3]. In total, 27 publications were included in the review (see Figure 3.1). These are presented and discussed in two sections: (1) Prevalence of ASD in the DS population, (2) The behavioural phenotype of DS and co-morbid ASD. Some publications are discussed in both sections.

Table 3.1 Literature review search terms and number of hits

Search term	Number of hits
Down AND syndrome AND autism	101
Down AND syndrome AND autistic	15
Trisomy AND 21 AND autism	1
Trisomy AND 21 AND autistic	0

[2] Four publications, although relevant, were excluded on the basis that they were reviews/commentary and not original research. A further 3 small scale intervention studies were excluded. One case study of a 14 year old DS male presenting with ASD was excluded due to a confirmed diagnosis of Fragile X syndrome.

[3] The literature search was not sensitive to several of the cited publications because they were papers which broadly investigated 'psychiatric disorders' in individuals with DS; thus the prevalence of ASD in DS, although reported, was not a primary focus. Other examples of publications missed by the literature search were early case studies. Cited conference papers were not followed up.

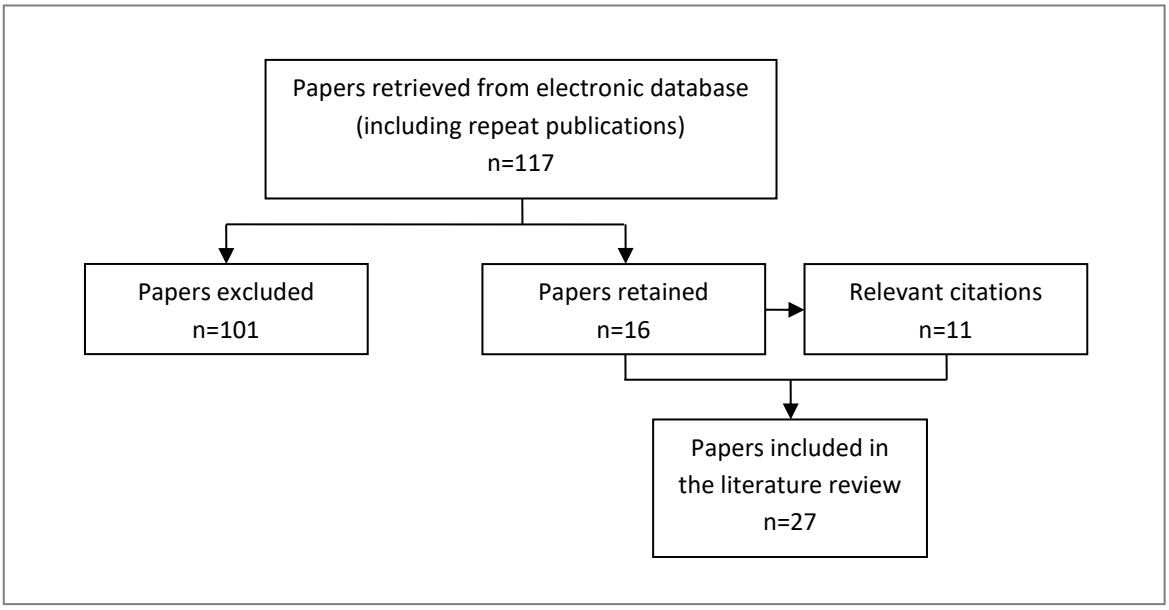

Figure 3.1 Flow chart of literature review search strategy

3.1 Prevalence of autism spectrum disorder in the Down syndrome population

To date, several studies have estimated the frequency of DS and co-morbid ASD; these are listed by date of publication in Table 3.2[4].

Small scale prevalence studies (n<50)

The identification of individuals with DS who show ASD characteristics began in the 1970s. An early epidemiological study of children with intellectual disabilities in London (UK) reported that one of a group of 28 children with DS showed 'social aloofness', a social impairment typically seen in ASD (Wing & Gould, 1979); however, the authors labeled the child as "non-autistic" (p.18). This was based on clinical judgment and may have been influenced by the belief at the time that DS and ASD were highly unlikely to co-occur (supported by psychiatric textbooks e.g. 'Child and Adolescent Psychiatry, Modern Approaches', Rutter & Hersov, 1985). A revised version of the instrument used in the study (the Medical Research Council's Handicaps, Behavior and Skills interview schedule [HBS]) has since been used to identify further cases of autistic type behaviour in DS. Lund (1988) found 5 adults out of a sample of 44 (11.4%) who displayed autistic behaviour and Turk and Graham (1997) reported 5 out of 45 children (11.1%). The HBS schedule is broad; however, certain aspects of the measure relate to the detection of ASD.

[4] Lowenthal et al. (2007), which is referenced in the text, was omitted from the table because the publication reported preliminary findings from the same sample used in Lowenthal et al. (2010).

Kent et al. (1999), using autism specific measures (the Asperger's Syndrome Screening Questionnaire [ASSQ] and the Childhood Autism Rating Scale [CARS]), identified 1 of 33 children with DS as having autism (3.0%) and a further 3 with ASD (12.1%). Starr et al. (2005) utilised the Autism Diagnostic Interview – Revised (ADI-R) and the Adapted Pre-Linguistic Autism Diagnostic Observation Schedule (A-PL-ADOS) with a group of 13 children with DS with low IQs (range 24-48) and reported that 5 (38.5%) may be considered to have ASD. In a similar study of 20 infants with DS, Hepburn et al. (2008) administered both the ADI-R and the Autism Diagnostic Observation Schedule – Generic (ADOS-G). Several children were reassessed again 2 years on. Two (10.0%) met criteria for autism and 3(15.0%) for ASD.

Larger scale prevalence studies (n>50)

A large scale investigation of adults with DS in Leicestershire (UK) only detected autism in 8 (2.2%) of 371 participants (Collacott et al., 1992). However, the focus of this study was on the occurrence of psychiatric disorders and the methodology was heavily reliant on medical records. A similar strategy was adopted by Hickey and Patterson (2006), who retrospectively reviewed the records of 248 children with DS who had attended a clinic in Cincinnati (USA), concluding that 15 (6%) met criteria for ASD. The first large scale investigation using an autism specific measure was conducted in Brazil by Lowenthal et al. (2007). A hundred and eighty individuals with DS were tested using the Autism Screening Questionnaire (ASQ), later renamed the Social Communication Questionnaire (SCQ). The sample was expanded to 228 and final prevalence statistics were published in 2010; 11 (4.9%) met the cut-off for autism and 33 (14.5%) met the cut-off for ASD (Lowenthal et al., 2010).

DiGuiseppi et al. (2010) used both the SCQ and the Modified Checklist for Autism in Toddlers (MCHAT); the majority of participants were also evaluated using the ADOS-G and the ADI-R. Of the 123 children screened, 77 completed the clinical evaluation. Although the screening test performance was good, with a combined sensitivity of 87.5% (95% CI: 66.6-97.7%), false positives were identified. The weighted prevalences of autistic disorder and total ASD were 6.4% and 18.2% respectively. Moss et al. (2013b) administered the SCQ to 108 individuals with DS as part of a larger project comparing aspects of the behavioural phenotypes of individuals with a range of genetic syndromes. Participants were recruited from the London and Birmingham areas through the UK Down's Syndrome Association. The application of the ASD and autism cut-offs to the SCQ scores resulted in estimated prevalence figures of 19.4% and 8.3% respectively.

Table 3.2 Overview of DS and co-morbid ASD prevalence studies (by publication date)

	Authors	Date	Measures	Sample size	Sample age[a]	Prevalence figure (n)	
						Autism	ASD
1	Wing & Gould	1979	HBS[1]	28	*Infant; Child*	0.0% (0)	3.6% (1)[†]
2	Gillberg et al.	1986	Psychiatric assessment; parent interview	20	*Child*	5.0% (1)	-
3	Lund	1988	HBS[1]	44	*Adult*	11.4% (5)	-
4	Collacott, Cooper, & McGrother	1992	Medical Records	371	*Adult*	2.2% (8)	-
5	Turk & Graham	1997	HBS[1]	45	*Infant; Child*	11.1% (5)	28.9% (13)
6	Kent et al.	1999	ASSQ[2]; CARS[3]	33	*Infant; Child*	3.0% (1)	12.1% (4)
7	Starr et al.	2005	ADI-R[4]; A-PL-ADOS[5]	13	*Child; Adult*	-	38.5% (5)
8	Hickey & Patterson	2006	Medical Records	248	*Infant; Child*	-	6.0% (15)
10	Hepburn et al.	2008	ADOS-G[6]; ADI-R[4]	20	*Infant*	10.0% (2)	15.0% (3)
11	DiGuiseppi et al.	2010	MCHAT[7]; SCQ[8]; ADOS-G[6]; ADI-R[4]	77	*Infant; Child*	6.4% (*)	18.2% (*)
12	Lowenthal et al.	2010	SCQ[8]	228	*Infant; Child*	4.9% (11)	14.5% (33)
13	Moss et al.	2013	SCQ[8]	108	*Infant; Child; Adult*	8.3% (9)	19.4% (21)

[a] '*Infant'* ≤ 5 years, '*Child'* 6-17 years, '*Adult'* ≥ 18 years; [†]Authors labeled the individual as 'non-autistic'; * Weighted percentage

[1] Handicaps, Behavior and Skills interview schedule (HBS; Wing & Gould, 1978; Wing, 1980)
[2] Asperger's Syndrome Screening Questionnaire (ASSQ; Ehlers & Gillberg, 1993)
[3] Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1986)
[4] Autism Diagnostic Interview – Revised (ADI-R; Lord et al., 1994)
[5] Adapted Pre-Linguistic Autism Diagnostic Observation Schedule (Berument et al., 2005)
[6] Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000)
[7] Modified Checklist for Autism in Toddlers (MCHAT; Robins, Fein, Barton & Green, 2001)
[8] Social Communication Questionnaire (SCQ; Rutter, Bailey & Lord, 2003), previously Autism Screening Questionnaire (ASQ; Berument et al., 1999)

Despite great variability in the estimations, which is likely to reflect differences in assessment measures, sample characteristics and changes in academic understanding and diagnostic criteria over time, the reported figures indicate a heightened prevalence in the DS population compared with the general population (see Chapter 2, Section 2.3).

3.2 Limitations of prevalence studies

Research measures

Several of the early prevalence studies used measures that were not specifically designed to detect autistic behaviours, such as the HBS. Although the HBS provides good insight into the social interaction skills of the individual, it does not assess the heterogeneous elements of ASD in fine detail. Collacott et al. (1992), as well as Hickey and Patterson (2006), did not employ an independent research measure but instead relied solely on the secondary source of medical records, which reduces the validity of their estimated prevalence statistics. The application of measures specifically designed to detect autistic characteristics is preferable. However, the demographic of the target population also needs to be taken into consideration. Kent et al. (1999) selected the ASSQ, an instrument designed for use with high functioning children on the autistic spectrum. Although it is syndrome specific, it is not suitable for individuals with DS who are characterised by cognitive impairment. The MCHAT or the SCQ are more appropriate depending on the age of the participants (DiGuiseppi et al., 2010; Lowenthal et al., 2010; Moss et al., 2013b).

Despite its strengths, it must be noted that the SCQ is an informant based questionnaire, which poses difficulties when assessing the accuracy of the identification of ASD. As outlined in the National Institute for Health and Clinical Excellence (NICE) guidelines on how to recognise and diagnose autism in children and young people, "tools to identify children and young people with an increased likelihood of autism (secondary screening) may be useful in gathering information about signs and symptoms of autism in a structured way but are not essential and should not be used to make or rule out a diagnosis of autism" (Baird, Douglas & Murphy, 2011, p.2). Best practice is to carry out autism specific observations (e.g. ADOS-G) and autism specific interviews (e.g. ADI-R). Direct observation of behaviour by a trained individual (with co-raters providing reliability scores), alongside a parent's perspective aided by the presence of a trained individual ensures a much greater degree of both validity and reliability. DiGuiseppi et al. (2010) employed all three forms of measure (informant based screening tool / direct observation / semi-structured interview) and thus produced the most valid prevalence statistics.

However, DiGuiseppi et al. (2010) did report a low specificity for the SCQ (see Chapter 11 for further discussion on the efficacy of the SCQ as a screening tool in the DS population).

Sample

The samples used in each study also need to be considered. Although Kent et al. (1999) and Hepburn et al. (2008) utilised autism specific measures, their sample sizes were small implying that their prevalence figures may not be representative of the DS population. DiGuiseppi et al. (2010), Lowenthal et al. (2010), and Moss et al. (2013b) all attained relatively good sample sizes. However, recruitment into these studies was restricted to defined geographical areas. Moreover, the level of non-response in these studies needs to be considered, as low response rates can lead to selection bias and the prevalence figures produced can deviate from the true population values. Lowenthal, et al. (2010) *(Curitiba, Southern Brazil)* achieved a strong participation rate of 88%, whereas DiGuiseppi et al. (2010) *(North Central Colorado, USA)* were less successful with a response rate of 30% (which reduced to 19% for clinical evaluations); Moss et al. (2013b) *(Birmingham and London, UK)* only utilised data from 22% of the study cohort. The accuracy of the given prevalence statistics also requires consideration. The confidence interval for the prevalence of ASD in DS reported by DiGuiseppi et al. (2010) is relatively large at 8.6% [18.2% (95% CI: 9.7%–26.8%)]. Neither Lowenthal et al. (2010) nor Moss et al. (2013b) report confidence intervals. However, calculations using the prevalence figures and sample sizes carried out on nQuery 4.0 put the confidence intervals at 4.6% [14.5% (95% CI: 9.9%-19.1%)] and 7.5% [19.4% (95% CI: 11.9%-26.9%)] respectively. This quantifies the closeness of the given figure to that of the unobserved population; a larger sample size would result in a smaller confidence interval indicating a more accurate prevalence figure.

The general age range of the sample (*infant / child / adult*) has been listed in Table 3.2. The reason for this is twofold. First, there is some indication that the onset of ASD characteristics is later in children with DS (Ji, Capone & Kaufmann, 2011). Therefore, in the studies utilising very young samples there may be some 'negative' cases which later develop ASD and thus become 'positive' cases. Second, a growing body of research indicates the increased risk of early onset dementia in DS (e.g. Holland et al., 2000; Tyrrell et al., 2001). Social interaction difficulties including diminished theory of mind, which is often associated with ASD, have been identified in dementia patients (Adenzato, Cavallo, & Enrici, 2010; Gregory et al., 2002). Therefore, studies which utilise adult samples may be falsely identifying social cognition deficits caused by dementia as ASD traits. This would result in adult samples producing inflated prevalence estimates. Lund et al. (1988)

recruited adults with DS over the age of 20. The mean age of the sample in the Collacott et al. (1992) study was 36.3 years (SD=11.2). The age range in the Moss et al. (2013b) study extended to 62 years. However, it is difficult to extrapolate the effects of these sample age ranges given the heterogeneity in the research methods.

The general ability of the samples also needs to be noted as a possible area of contention. Many of the studies did not utilise a measure of intelligence and/or adaptive skills. Nevertheless, comparison of the Starr et al. (2005) and Hepburn et al. (2008) papers highlights a possible disparity in prevalence estimates on the basis of developmental functioning. The Starr et al. (2005) sample appeared to be a lower functioning group and more cases of ASD were identified in this group despite similar autism specific measures being used in both studies. However, the measures of general ability differed and there were other sample discrepancies such as age.

3.3 The behavioural phenotype of Down syndrome and co-morbid autism spectrum disorder

Section 3.3.1 Case studies of autism spectrum disorder in Down syndrome

Early reports of the characteristics of DS and co-morbid ASD focused on individual cases. In total there are 20 case studies available in the literature, which are listed by date of publication in Table 3.3[5].

A thematic analysis of the phenotypic descriptions of the individuals was carried out. 'Themes' were based on clinical characteristics. If a characteristic was present in 2 or more of the individuals it was included in the analysis. Table 3.3 outlines the presence or absence of each characteristic in the individual cases (presence is indicated by a black tick), and the overall percentage occurrence of the characteristics in the group as a whole. The vast majority of cases had low levels of general functioning, showed marked language deficits and were socially aloof or withdrawn. Stereotyped behaviours and repetitive, ritualistic play were also common. In terms of challenging behaviours, half of the cases were aggressive and a fifth displayed self-injurious behaviour.

[5] Starr et al. (2005) provided written descriptions of 6 individuals; however, the first of these cases only displayed ASD characteristics briefly during early development and therefore is excluded from the current review.

Table 3.3 A thematic analysis of the phenotypic descriptions within case studies of individuals with DS and co-morbid ASD

Authors	**Case**	**Themes**											
		Low IQ / general functioning	Language delay/ impairment	Social aloofness/ withdrawal	Stereotyped behaviour	Repetitive play / rituals/ restricted interests	Impaired eye gaze	Attachment to objects	Aggression	Impaired motor function	Self-injury	Hyperactivity	Regression in skills
Wakabayashi (1979)	1	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓
Bregman & Volkmar (1988)	2	✓	✓	✓	✓		✓		✓				
Ghaziuddin & Ghaziuddin (1992)	3	✓		✓	✓	✓							
	4	✓	✓	✓	✓	✓	✓						
	5	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	
Howlin et al. (1995)	6	✓	✓	✓	✓	✓	✓	✓	✓	✓			
	7	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	
	8	✓	✓	✓	✓	✓	✓	✓	✓				
	9	✓	✓	✓	✓	✓	✓	✓	✓				
Ghaziuddin (1997)	10	✓	✓	✓	✓	✓	✓	✓					
	11	✓	✓	✓	✓	✓	✓						
	12	✓	✓	✓	✓	✓	✓	✓					
Kent et al. (1999)	13	✓	✓	✓	✓	✓	✓	✓	✓		✓		
	14	✓	✓	✓	✓	✓	✓	✓	✓		✓		
	15	✓	✓	✓		✓	✓	✓	✓				
Starr et al. (2005)	16	✓	✓	✓		✓				✓			
	17	✓	✓	✓		✓		✓					
	18	✓	✓	✓	✓	✓							
	19	✓	✓	✓	✓	✓							✓
	20	✓	✓		✓								
Percentage Occurrence		100%	95%	95%	85%	85%	70%	60%	50%	20%	20%	15%	10%

Although this thematic analysis gives insight into the behavioural phenotype of the co-morbidity, the findings must be treated with caution as the descriptions utilised were written by varying authors, who may have different experiences, perspectives and focuses. It may be the case that an individual displayed certain behaviours but the author did not note them down due to specific research priorities. For example, case number 12 (Ghaziuddin, 1997) was noted to have shown *'ongoing behavioural problems'* which may have included aggression and self injury. However, as these behaviours were not specifically mentioned they were not included in the analysis.

Section 3.3.2 Systematic investigation of autism spectrum disorder in Down syndrome

Although case studies provide useful insight into the co-occurrence of DS and ASD, in order to establish a clear behavioural phenotype of the co-morbidity, a more systematic research approach needs to be adopted and statistical trends identified. Systematic studies are listed in Table 3.4 by date of publication.

Consistent findings

When compared with individuals with DS only, individuals with DS and co-morbid ASD consistently display poorer cognitive functioning (Carter et al., 2007; Magyar et al., 2012; Molloy et al., 2009; Rasmussen et al., 2001) and adaptive behaviour skills (Dressler, 2011; Magyar et al., 2012; Molloy et al., 2009). Moreover, repetitive and stereotyped behaviours are constantly reported as more common in this group (Capone et al., 2005; Carter et al., 2007; Hepburn & Maclean, 2009; Ji, Capone & Kaufmann, 2011; Moss et al., 2013b). Increased levels of hyperactivity, too, is a regular finding that differentiates individuals with DS and co-morbid ASD from individuals with DS only (Capone et al., 2005; Carter et al., 2007; Dressler et al., 2011; Ji et al., 2011; Moss et al., 2013b). Rasmussen et al. (2001) noted, through inspection of a group of individuals with the co-morbidity, that infantile spasms were common. Molloy et al. (2009) supported this by detecting more cases of children who suffered from seizures in a DS and co-morbid ASD group than a DS only group.

Table 3.4 Overview of studies investigating the behavioural phenotype of DS and co-morbid ASD

	Authors	Date	Measures	Sample(s)	Main findings[a]
1	Rasmussen et al.	2001	Interview; CARS[1]; ABC[2]; Griffiths Mental Development Scales[3]; Wechsler Intelligence Scales[4]	25 DS+ASD	Delay in diagnosis. History of autistic disorders in family. Low intellectual level, infantile spasms, early hypothyroidism and brain injury after major heart surgery all common.
2	Capone et al.	2005	ABC[2]	131 DS (61 +ASD; 26 +SMD; 44 typical DS)	DS+ASD group higher levels of irritability, lethargy/social withdrawal, stereotypy and hyperactivity.
3	Carter et al.	2007	ABC[2]; Autism Behavior Checklist[5]	127 DS (64 +ASD; 19 +SMD; 18 +DB; 16 typical DS)	DS+ASD group lower IQ/IQ equivalent, higher levels of irritability, lethargy/social withdrawal, stereotypy, hyperactivity and inappropriate speech.
4	Castillo et al.	2008	ADI-R[6]	12 ASD; 12 DS+ASD	Regression occurs later in children with DS+ASD.
5	Hepburn & Maclean	2009	ADI-R[6]; SCQ[7]; ADOS-G[8]; MSEL[9]; DAS[10]; Vineland II[11]; DBC-P[12]	54 typical DS; 22 DS+ASD; 34 DD	DS+ASD group higher levels of overall problem behaviours, self-absorbed and poor social relating skills. More repetitive behaviours.
6	Molloy et al.	2009	ADI-R[6]; MSEL[9]; Vineland II[11]	20 Trisomy 21; 20 Trisomy 21+ASD	DS+ASD group lower levels of cognitive ability and adaptive behaviour skills (communication, daily living, and socialisation). Increased risk of seizures.
7	Dressler et al.	2011	Vineland II[11]; CARS[1]	8 typical DS; 8 DS+ASD; 8 ASD	DS+ASD group lower levels of adaptive behaviour skills (communication, daily living, and socialisation). Higher levels social relating difficulties, emotional disturbance and hyperactivity.
8	Ji et al.	2011	ABC[2]; Autism Behavior Checklist[5]; various cognitive tests[13]	293 DS (114 +ASD; 43 +SMD; 104 +DB; 32 typical DS)	DS+ASD group display higher levels of irritability, lethargy/social withdrawal, stereotypy, hyperactivity and inappropriate speech. Late onset of ASD symptoms.

9	Magyar, Pandolfi & Dill	2012	SCQ[7];ADI-R[6]; Vineland II[11]	38 typical DS; 33 DS+ASD	DS+ASD group lower levels of cognitive ability and adaptive behaviour skills (communication, daily living, and socialisation)
10	Moss et al.	2013	SCQ[7]; Wessex[14]; MIPQ-S[15]; TAQ[16]; CBQ[17]; RBQ[18]	17 typical DS; 17 DS+ASD; 17 ASD	DS+ASD and ASD-only groups showed more stereotyped behaviour, repetitive language, overactivity and self-injury. DS+ASD and DS-only groups appeared less withdrawn from their surroundings.

[a]Comparisons (i.e. higher / lower) are relative to children with DS only

DS =Down syndrome; ASD =autism spectrum disorder; SMD =stereotypic movement disorder; DB =disruptive behaviour; DD =developmental disorder

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[1] Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1986)
[2] Aberrant Behavior Checklist (ABC; Aman et al., 1985)
[3] Griffiths (1970)
[4] Wechsler (1992)
[5] Krug, Arick & Almond (1980)
[6] Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter & Couteur, 1994)
[7] Social Communication Questionnaire (SCQ; Rutter, Bailey & Lord, 2003)
[8] Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000)
[9] Mullen Early Scales of Learning (MSEL; Mullen,1995)
[10] Differentiated Abilities Schedule (DAS; Eliot, 1990)
[11] Vineland Adaptive Behavior Scales, second edition (Vineland II; Sparrow, Balla & Cicchetti (2005)
[12] Developmental Behavior Checklist-Primary carer report (DBC-P; Einfeld & Tonge, 1995)
[13]Wechsler Intelligence Scales (Wechsler, 1992)
Bayley Scales of Infant Development (Bayley, 2006)
Stanford Binet Intelligence Scale (Roid, 2003)
Vineland Adaptive Behaviour Scale (Sparrow at al., 2005)
Woodcock–Johnson achievement test (Mather & Woodcock, 2001)
[14] Wessex Questionnaire (Kushlick et al., 1973)
[15] The Mood Interest and Pleasure Questionnaire-Short (MIPQ-S; Ross & Oliver, 2003)
[16] The Activity Questionnaire (TAQ; Burbidge et al. 2010)
[17] The Challenging Behaviour Questionnaire (CBQ; Hyman, Oliver, & Hall, 2002)
[18] The Repetitive Behaviour Questionnaire (RBQ; Moss et al. 2009)

Findings requiring further validation

Castillo et al. (2008) investigated regression in children with DS and co-morbid ASD and found that the age at regression was substantially higher than in an idiopathic ASD group. Castillo et al. (2008) state that "many individuals with a dual diagnosis of autism and Down syndrome have a history of developmental regression" (p.89). Although Castillo et al. (2008) do not report data on the frequency of occurrence of regression, their statement is validated by a substantial proportion (54%) of children in a previous DS and co-morbid ASD cohort reportedly showing a regression in skills (data from a conference paper not included in this review; see Castillo et al., 2008).

Moss et al. (2013b) report significantly more self-injurious behaviour in individuals with DS who screen positive for ASD (opposed to individuals with DS who screen negative). Although self-injury was identified in several case studies of DS and co-morbid ASD (see Section 3.3.1), no further systematic studies have investigated the presence of the behaviour.

Conflicting findings

Some divergence is seen in reports of anxious behaviour in individuals with DS and co-morbid ASD. Carter et al. (2007) report comparatively high levels of anxiety in this group when compared to individuals with DS only. However, other studies report no group difference (Dressler et al., 2011; Hepburn & Maclean, 2009). Each study utilised a different measure of anxiety, which may have contributed to the variance in findings. Carter et al. (2007) conducted a single item analysis of anxiety (i.e. Autism Behavior Checklist item: *'often frightened or very anxious'*). Dressler et al. (2011) adopted a similar strategy using an item from the CARS, but with much smaller group numbers. Despite the small sample sizes Dressler et al. (2011) found significant findings on several of the other CARS items. Hepburn and Maclean (2009) used the anxiety subscale of the Developmental Behaviour Checklist (DBC) with decent sample sizes (subscale items include: *'distressed about being alone'*, *'cries easily for no reason, or over small upsets'* and *'has nightmares, night terrors or walks in sleep'*). This method is likely to have provided a more reliable picture of anxious behaviour. However, further investigation is needed to elucidate whether anxious behaviour is integral in the DS and co-morbid ASD phenotype.

In a similar vein, some studies have identified lethargy/social withdrawal as more common in individuals with DS and co-morbid ASD than individuals with DS only (Capone et al., 2005; Carter et al., 2007; Ji et al., 2011). In contrast, Moss et al. (2013b)

found that individuals with DS who screened positive for ASD were just as interested in their surroundings as those who screened negative, and both groups related more to their environment than an idiopathic ASD group. It must be noted that the 3 studies that report higher levels of lethargy/social withdrawal all used the same measure (Aberrant Behavior Checklist) and were conducted in the same clinic, and so participants may be shared across the samples. These similarities could have contributed to the consistent finding. On the other hand, the groups in the Moss et al. (2013b) study were small and determined by the SCQ only. It may be the case that by using a different measure (Mood Interest and Pleasure Questionnaire) Moss et al. (2013b) were measuring a different construct.

A final area of contention is the rate of disruptive behaviour in this group. Ji et al. (2011) identified disruptive behaviour as a core characteristic of a DS and co-morbid ASD group (more so than other DS groups). However, Hepburn and Maclean (2009) reported no difference in the level and disruptive / antisocial behaviour between groups of DS children with and without ASD.

Comparisons with idiopathic ASD

Few of the systematic studies have made comparisons with idiopathic ASD (Castillo et al., 2008; Dressler et al., 2011; Moss et al., 2013b). Dressler et al. (2011) indicated similarity between ASD in the co-morbid presentation and idiopathic ASD (e.g. social relating difficulties and emotional disturbance). However, expressive language was identified as a weaker attribute for the DS and co-morbid ASD group on both the Vineland II and the CARS. The DS and co-morbid ASD group were also reported to have greater difficulty with change and to display higher levels of hyperactivity than the idiopathic ASD group. Other than greater interest in the environment among individuals with DS who screened positive for ASD, Moss et al. (2013b) did not identify any other differences to the idiopathic ASD group across measures of autism characteristics, mood, repetitive behaviour levels of activity and challenging behaviour. Nevertheless, group sizes across these studies were very small.

3.4 Limitations of behavioural phenotype studies

Sample

Although some studies have achieved large numbers in their comparison groups (e.g. Capone et al., 2005; Carter et al., 2007; Ji et al., 2011), others have very small samples (e.g. Castillo et al., 2008; Dressler et al., 2011; Moss et al., 2013b). This limits statistical

power to detect group differences and, as a result, it is possible that more subtle group differences were not detected. The wide age range of some samples (e.g. Moss et al., 2013b) also raises concerns given that behavioural changes can occur over the life-course (e.g. possible effects of dementia, see Section 3.2 for further details).

Research measures

In order to achieve a global understanding of behaviour a range of appropriate measures is required. In some cases, broad behaviour scales, such as the ABC, Autism Behavior Checklist and CARS have been selected (e.g. Capone et al., 2005; Carter et al., 2007; Dressler et al., 2011; Ji et al., 2011). Although useful, they are not detailed enough to provide a full understanding of the phenotype of DS and co-morbid ASD. More in-depth measures have been utilised by some; for instance, Castillo et al. (2008) and Molloy et al. (2009) both conducted comparative studies using the ADI-R. Yet, Castillo et al. (2008) used the measure in isolation, with a small sample size and focussed specifically on the age at regression of children with ASD with and without DS. Molloy et al. (2009) only coupled the ADI-R with ability measures. Plus, although the ADI-R does provide greater insight than questionnaire methods, it is still informant-based. Direct observation of the individuals with DS and autistic characteristics would enrich the understanding of the behavioural phenotype further. Hepburn and MacLean (2009) used the ADI-R and ADOS to classify children but only reported group differences on informant measures of challenging and repetitive behaviour. Moss et al. (2013b) explored more specific aspects of the phenotype, such as ability, hyperactivity, repetitive behaviour, mood and challenging behaviour. This gave a broader understanding of the group. However, the measures used were relatively circumscribed and solely informant-based.

3.5 Why study Down syndrome and co-morbid autism spectrum disorder further?

Despite initial beliefs that the association was very rare (Rutter & Hersov, 1985), recent research shows that a substantial proportion of children with DS also meet diagnostic criteria for an ASD. It has been estimated that 6-19%[6] of people with DS have social interaction impairments meeting criteria for ASD (DiGuiseppi et al., 2010; Hickey & Patterson, 2006; Lowenthal et al., 2010; Moss et al., 2013b). This indicates a highly elevated risk of the disorder in the DS population compared with the general population, in

[6] Figures taken from larger scale prevalence studies (i.e. n>50) (see Table 3.2)

whom the risk is around 1% (Brugha et al., 2011; Baird et al., 2006). These figures are likely to be influenced by the sample size, age range of sample and the instruments employed in each of the studies. However, from the given figures we can infer that DS and co-morbid ASD is currently under-diagnosed by clinical professionals. If a larger sample size were screened a more statistically accurate prevalence estimate could be determined. Moreover, a larger scale study may clarify whether the heavily male gender ratio seen in idiopathic ASD (Fombonne, 2003) is seen in DS and co-morbid ASD. To date male overrepresentation has not been identified in this group (e.g. Lowenthal et al., 2007; Moss et al., 2013b).

Often it is the case that emotional and behavioural difficulties faced by these children are attributed to their existing diagnosis of DS and many parents experience major difficulties in obtaining an autism diagnostic assessment (Patterson, 1999). This propensity to ascribe *all* the behaviours of an individual to the genetic syndrome which they have an existing diagnosis for, referred to as 'diagnostic shadowing', has been noted as common in other groups (Moss & Howlin, 2009). It is of paramount importance that if a child displays autistic type behaviours appropriate advice and educational provision is made available. The behavioural phenotypes of the two disorders (DS and ASD) show great variance. Most notably, ASD impairs social interaction whereas individuals with DS are often described as very social. In order to best advise families of children with the co-morbidity, a specific behavioural profile needs to be established. Many previous studies (e.g. Capone et al., 2005; Carter et al., 2007; Dressler et al., 2011; Ji et al., 2011) have utilised broad behaviour scales which are not expansive enough to fully understand the co-morbidity. Further investigation of the behavioural expressions of these children is needed. Plus, in order to advise on educational provision it is important to gauge an understanding of the appropriateness of current provision, and to measure behaviour outcomes at school as well as at home.

Moreover, the evaluation of ASD in genetic syndromes has highlighted that the presentation of specific ASD characteristics, which can be referred to as the 'autism profile', may be atypical with subtle but qualitative differences noted when compared with idiopathic ASD (Moss & Howlin, 2009). Thus, in order to aid clinicians in the diagnostic process, investigation of the specific presentation of autism characteristics in children with DS is needed.

Further to this, it is important to note that studies in this area have focused on overall group differences. However, it seems that there may be individual variability with some children with the co-morbidity being more severely impaired than others. Thus far

there has been no attempt to study individual differences among children with DS and co-morbid ASD.

Finally, with the struggle of parents being recognised in the field (Patterson, 1999), there is a need to investigate the impact of raising a child with the co-morbidity and the particular difficulties that these families face; to date this has not been systematically investigated.

Not only will research into DS and co-morbid ASD inform clinical practice relating to the co-morbidity, but there are also research implications. At present children with DS are frequently included in studies as control participants for comparison with children with ASD. The recognition of the co-occurrence of the disorders should lead a more valid appointment of controls in future studies.

3.6 Contributions of the current study

The current study will contribute to the field of research by providing:

- Data on the *frequency of autistic-type behaviours in a large sample* of children with DS aged 6-15 years.
- Analysis of the *autism profile* of children with DS and autistic-type behaviours compared with children with idiopathic ASD.
- Exploration of the *emotional and behavioural problems* experienced by children with DS and autistic-type behaviours *both at home and at school*.
- Information on the *incidence and age of regression* in children with DS and autistic-type behaviours.
- Insight into the *appropriateness of educational placements* for children with DS and autistic-type behaviours.
- *Detailed observational data* on *behaviour problems* and *autism characteristics* in children with DS and autistic-type behaviours.
- Recognition of *individual variability* in children with DS and autistic-type behaviours.
- Finally, the thesis will also explore the *impact on the family* of raising a child with DS and autistic-type behaviours, on both parents and siblings.

Chapter 4: Overview of challenging behaviour in Down syndrome and autism spectrum disorder

Outline:
This chapter provides a definition of 'challenging behaviour', outlines the functional analysis approach to modifying challenging behaviour and briefly summarises challenging behaviour in Down syndrome, autism spectrum disorder, and the co-morbidity.

4.1 Defining challenging behaviour

Emerson (2001) defines challenging behaviour as: *"Culturally abnormal behaviour(s) of such an intensity, frequency or duration that the physical safety of the person or others is likely to be placed in serious jeopardy, or behaviour which is likely to seriously limit use of, or result in the person being denied access to, ordinary community facilities."* It can include aggressive behaviour, self-injury, damage to property, a range of socially inappropriate behaviours such as screaming or hand flapping, as well as other more 'resistant' types of behaviour including refusal to participate in activities.

4.2 A functional analysis approach to modifying challenging behaviour

The functional analysis approach to intervening in challenging behaviour focuses on the assessment of the behaviours in terms of frequency, duration, severity of any damage, the circumstances in which they occur and the impact on the individual or on those around them. Functional analysis aims to determine exactly what the behaviours are - it is not adequate, for example, to say that the person is 'aggressive'; the behaviour needs to be described in detail, along with the circumstances in which the behaviour tends to occur. Often people with challenging behaviour demonstrate more than one form of behaviour, and all of these need to be considered. Although carer reports are useful, direct observation is also needed to understand more about the causes and possible interventions for the behaviours. The *antecedents* to the target behaviour are considered (i.e. what was going on before the behaviour occurred), the *behaviour* itself, and the *consequences* of the behaviour (i.e. what the person and the others around them did afterwards). This is referred to as the ABC approach.

The National Institute for Health and Care Excellence (NICE) guidelines for the management of autism refer to a functional analysis approach to challenging behaviour.

The guidelines state that *'when deciding on the nature and content of a psychosocial intervention to address challenging behaviour, use a functional analysis'* (Section 1.5.3, NICE, 2012). It states that functional analysis provides information on: *'factors that appear to trigger the behaviour* [and] *the consequences of the behaviour (that is, the reinforcement received as a result of the behaviour)'* and identifies *'trends in behavioural occurrence, factors that may be evoking that behaviour and the needs that the person is attempting to meet by performing the behaviour'.*

In the present study challenging behaviour within the behavioural phenotype of Down syndrome (DS) and co-morbid autism spectrum disorder (ASD) will be considered. The functional approach will be adopted in the sense that as much detail will be sought as possible about the different forms of challenging behaviour. For instance, rather than just considering 'repetitive behaviour' in its broadest form, the varying topographies of repetitive behaviour will be investigated. This research study critically explore the established view that repetitive behaviour is more common in children with DS and co-morbid ASD than children with DS only (Capone et al., 2005; Carter et al., 2007; Hepburn & Maclean, 2009; Ji et al., 2011) and attempt to 'cast a magnifying glass' over the different forms of challenging behaviour described. Parent and teacher reports on challenging behaviour will be augmented by a natural observation of challenging behaviour within the school context, and parents will be questioned about their perception of the function of their child's challenging behaviour (see Chapter 8 for more detail on the group study methodology).

4.3 Challenging behaviour in Down syndrome

A number of problem behaviours are typically described in children with DS. For instance, many are depicted as stubborn, inattentive and impulsive (Dykens, 2007) but such problems may often stem from their difficulties in concentrating and low levels of task persistence (Fidler, 2005). Oppositional behaviours are frequently described; a common context in which oppositional behaviour is met by parents and carers is at bedtime - children with DS have been found to show more resistance to going to bed than typically developing children matched for chronological age (Carter et al., 2009). Despite this, when compared with children with autism spectrum disorder (ASD) and children with mixed aetiology intellectual disabilities who are matched for chronological age, gender and communication skills, children with DS have been found to display *less* severe behavioural problems (Griffith et al., 2010).

4.4. Challenging behaviour in autism spectrum disorder

Behavioural problems are common in children with ASD. Infants with ASD, with and without intellectual disability, are reported to display higher levels of emotional and behavioural problems than typically developing children (Totsika et al., 2011). These problems appear to persist throughout childhood and adolescence (Simonoff et al., 2013). Maskey et al. (2013) report that although some challenging behaviours seen in children with ASD (e.g. hyperactivity and self injury) are associated with lower ability, others (e.g. anxiety and aggression) are common regardless of ability or age. When directly compared with children with a confirmed diagnosis of DS, who were matched on chronological age, gender and communication skills, children with ASD were rated as having more problem behaviours, especially in relation to anxiety and self-injury, and lower levels of social competence (Griffith et al, 2010). These emotional and behavioural problems in ASD have been found to contribute significantly to raised levels of stress and mental health issues faced by mothers, even more so than the diagnosis itself (Herring et al., 2006) (see Chapter 5 for further information on the impact on families).

4.5 Challenging behaviour in Down syndrome and co-morbid autism spectrum disorder

As noted in Chapter 3, individuals with DS and co-morbid ASD are consistently reported as demonstrating higher levels of repetitive and stereotyped behaviours and hyperactivity than individuals with DS only (Capone et al., 2005; Carter et al., 2007; Dressler et al., 2011; Hepburn & Maclean, 2009; Ji et al., 2011; Moss et al., 2013b). Moss et al. (2013b) also report more self-injurious behaviour in individuals with DS who screen positive for ASD (opposed to individuals with DS who screen negative). Although self-injury has been reported in several case studies of DS and co-morbid ASD (see Section 3.3.1), there have been no further systematic studies of this behaviour. Data on rates of disruptive behaviour in this group are conflicting. Ji et al. (2011) identified disruptive behaviour as a core characteristic of a DS and co-morbid ASD group (more so than other DS groups). In contrast, Hepburn and Maclean (2009) reported no difference in the level and disruptive / antisocial behaviour between groups of DS children with and without ASD.

Chapter 5: Overview of the impact on the family

Outline

This chapter provides an overview of research into parent stress and sibling adjustment within families of children with Down syndrome and children with autism spectrum disorder.

5.1 Parent stress

Section 5.1.1 Defining parent stress

Parental stress can be defined as 'the experience of distress or discomfort that results from demands associated with the role of parenting' (Deater-Deckard, 1998). Yet, general models of stress consider the interaction of the individual with the environment (Folkman & Lazarus, 1985). Therefore, additional environmental stressors, as well as the role of parenting, should be considered when conceptualising parent stress.

Although higher levels of stress are reported by parents of children with developmental disabilities (Baker et al., 2003; Gupta, 2007), it is important not to assume a direct association between the presence of stress and the child's disability but to consider other potential stressors. Furthermore, developmental disabilities can be heterogeneous; therefore it is important to consider individual child characteristics, such as functional ability and challenging behaviour, when investigating stressors.

In addition to environmental stressors, there are mediating factors that can amplify stress (Webster-Stratton, 1990). For instance, the psychological morbidity of the parent may affect the level of perceived stress. Yet, the association between stressors and mediators is bidirectional as the presence of stress may also affect the psychological morbidity of the parent. It is of particular importance to consider psychological morbidity when utilising self-report measures as the presence of dysfunction may affect ratings, although Griffith et al. (2010) reported no effect of maternal psychopathology on ratings of child behaviour.

Section 5.1.2 The importance of studying parent stress

It is important to investigate parent stress levels and potential stressors across disability groups as the findings may be suggestive of the need for intervention, as well as the form of approach to take. For instance, if the high level of challenging behaviour associated with

autism spectrum disorder (ASD) is perceived as a source of parent stress, then intense early intervention for early childhood challenging behaviour could be implemented as a preventative step to reduce parent stress.

Reducing parent stress may not only benefit the parent, but also the child; Hastings (2002) proposes a cyclical model in which stress adversely affects parenting behaviour (see Figure 5.1). The association between parental stress and parenting behaviour has received little research attention. However, Karrass, Van Deventer and Braungart-Rieker (2003) found that mothers who reported more stress were less likely to read to their child, indicating a causal relationship between stress and parenting behaviour.

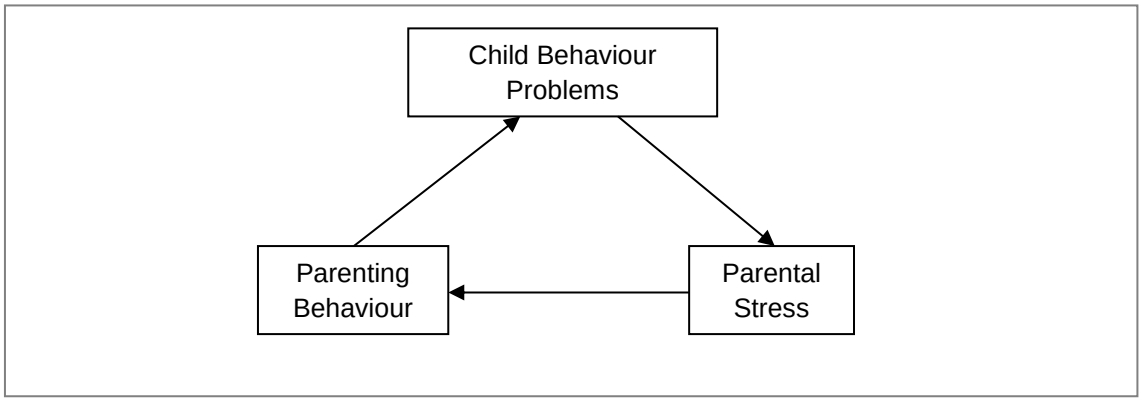

Figure 5.1 Hastings' (2002) model of the relationships between parenting stress, parent behaviour, and child behaviour problems

Section 5.1.3 Parent stress associated with having a child with Down syndrome

The term "Down syndrome advantage" (Esbensen & Seltzer, 2011) has been coined due to the extensive body of research that indicates parents of children with Down syndrome (DS) experience lower levels of stress than parents of children with other developmental and intellectual disorders (e.g. Griffith et al., 2010, Kasari & Sigman, 1997), and are no more likely to suffer from depression than parents of typically developing children (e.g. Van Riper, Ryff & Pridham, 1992). Although the bulk of evidence supports this "advantage", it must be noted that some studies report similar levels of psychological well-being between parents of children with DS and parents of children with other disabilities (Greenberg et al., 2004; Roach, Osmond & Barratt, 1999). However, these studies are in the minority.

It has been considered whether the "advantage" can be attributed to contextual variables. For instance, maternal age is a contributory factor in the aetiology of DS and therefore DS parental groups in comparative studies are often likely to be older. One could

hypothesise that with age comes greater life experience and coping skills, as well as an increased chance of a higher income and marital stability. These are all possible contributory factors to a lower level of stress. The literature on this theory is split; there has been some evidence of the "advantage" disappearing once such contextual factors are controlled for (Abbeduto et al., 2004), yet some evidence that the "advantage" remains true (Eisenhower, Baker & Blacher, 2005).

Other research in this area has focussed on the role of the behavioural phenotype of DS on levels of parent stress. Children with DS tend to be social and affectionate (Dykens, 1999) and parents of children with DS tend to perceive their children as less difficult than parents of children with other developmental disabilities, such as autism (Griffith et al., 2010). A within-group study, focussing only on mothers of children with DS, found that the child having fewer behavioural problems contributed the most to better maternal outcomes. The functional ability of the child was also considered; however, it was the behaviour element of the phenotype that predicted maternal well-being most strongly (Esbensen & Seltzer, 2011).

Perceived support has been identified as a possible reason for the "advantage". Parents of children with DS are reported as having more extensive and satisfying networks of support than other parent groups (Hauser-Cram et al., 2001), and have access to syndrome-specific support groups such as the Down's Syndrome Association (DSA). It has been reported that syndrome-specific support groups can lead to more adaptive coping (Erickson & Upsur, 1989). However, other parent groups also benefit from syndrome-specific support groups, such as The National Autistic Society for parents of children with ASD. Siklos and Kerns (2006) assessed the need for social support in parents of children with DS and parents of children with ASD. The parent groups did not differ on the number of important needs reported, or the number of important needs being met. However, they did differ in the types of support they most frequently endorsed as *important* or *unmet*.

Section 5.1.4 Parent stress associated with having a child with autism spectrum disorder

Parents of children with ASD report more parent stress (Eisenhower et al., 2005) and generally poorer quality of life (in relation to physical health, psychological health and social relationships) (Mugno et al., 2007) than parents of children with other developmental disorders. Due to the unclear aetiology of ASD, the absence of physical differences when compared with typically developing children and the general ambiguity surrounding the disorder, Siman-Tov and Kaniel (2011) suggest that feelings of uncertainty may be reinforced in parents of children with ASD and thus levels of stress are raised.

ASD symptom severity of the child, child behaviour and the perceived amount of support have been found to affect the level of stress and depression in parents of children with ASD (Benson, 2006; Benson & Karlof, 2009; Herring et al., 2006; Meltzer, 2011; Siman-Tov & Kaniel, 2011). Interestingly, Benson (2006) found that social support had a greater positive impact on parent well-being when the child's ASD symptom severity was lower.

The Broader Autism Phenotype (BAP; Folstein & Rutter, 1977) has also been reported as a predictor of parental depression (Ingersoll & Hambrick, 2011). The BAP is a set of behaviours qualitatively similar to ASD which are found more commonly in relatives of individuals with ASD than in the general public. The presence of these behaviours has been associated with reduced social support and maladaptive coping strategies, which in turn have been strongly associated with parent stress and depression (Ingersoll & Hambrick, 2011).

Sleep disruption has been identified as a potential mechanism for increased levels of depressive symptoms in parents of children with ASD; child sleep quality was a contributory factor to maternal depressive symptoms and paternal sleep quality was a contributory factor to parent depressive symptoms (Meltzer, 2011).

Section 5.1.5 Parent stress associated with having a child with Down syndrome and co-morbid autism spectrum disorder

To date, there has been no research into stress among parents of children with DS and co-morbid ASD. Due to maternal age being a contributory factor in the aetiology of DS, parents in this group are likely to be older and therefore could benefit from certain contextual variables (e.g. life experience, coping skills, higher income and marital stability). However, the sociability and relatively low level of behavioural problems associated with the DS phenotype may be affected by the presence of the co-morbid ASD, which in turn may affect the stress experienced by parents. Furthermore, although this parent group will have access to DS specific support groups, the differing needs of parents of children with DS and co-morbid ASD may not be met by such groups, resulting in a lower rate of perceived support.

Summary:

- Most research indicates that parents of children with DS experience lower levels of stress than parents of children with other developmental disorders.
- In contrast, parents of children with ASD tend to report more stress than parents of children with other developmental disorders.
- Many factors are negatively associated with parent well-being. These include: severity of child's behaviour problems, functional disability and ASD symptoms; parents having symptoms associated with the Broader Autism Phenotype and sleep disruption.
- Parent wellbeing is positively associated with perceived support.

5.2 Sibling adjustment

Section 5.2.1 Defining sibling adjustment

In the present study, sibling adjustment refers to the level of behavioural and emotional problems reportedly experienced by the sibling of a child with a developmental disorder, in this case DS (with and without ASD). Factors such as the age and gender of each child and the age difference between the sibling and the child with the developmental disorder should all be considered.

Section 5.2.2 The importance of studying sibling adjustment

It is important to investigate sibling adjustment in families of children with developmental disorders because sibling relationships are an important context for social and emotional development (Whiteman, Becerra-Bernard & Jenson, 2011) and dysfunction within the relationship may lead to social and emotional problems. The low functional ability of many children with developmental disorders means that in adulthood their siblings are likely to become their carers (Dew, Llewellyn & Balandin, 2004). Therefore, the issue of how children respond to the experience of living with a sibling with a developmental disorder is pertinent.

Section 5.2.3 Adjustment of siblings of children with Down syndrome

Parent reports tend to indicate that the siblings of children with DS are socially competent and have a low incidence of behaviour problems, no different to that of siblings of typically developing children (Cuskelly, Chant & Hayes, 1998; Cuskelly & Gunn, 2006;

Van Riper, 2000). However, there has been some indication of increased conduct problems in girls who have a sibling with DS (Cuskelly & Gunn, 1993). Research into the experience of having a sibling with DS indicated that the vast majority of older siblings felt that they were better people because of their brother or sister with DS. However, a minority felt that their parents gave too much attention to the child with DS. Siblings were more likely to feel this way if they were under the age of 13 or were the same sex as the DS child (Skotko, Levine & Goldstein, 2011).

Section 5.2.4 Adjustment of siblings of children with autism spectrum disorder

Studies on the behavioural and emotional adjustment of siblings of a child with ASD yielded mixed results. Compared with normative data, siblings of children with ASD were reported to show more peer problems, more overall adjustment problems and lower levels of prosocial behaviour (Hastings, 2003). Compared with siblings of typically developing children, siblings of a child with ASD were reported to show higher levels of internalising and externalising problems (Rodrigue, Geffken & Morgan, 1993), and higher levels of inattention/hyperactivity and conduct problems (Bägenholm & Gillberg, 1991). However, other research has indicated no difference in the adjustment of siblings of children with ASD and siblings of typically developing children (Gold, 1993; Kaminsky & Dewey, 2002). No differences were found when the siblings of children with ASD were compared with the siblings of children with DS (Rodrigue et al., 1993).

Hastings (2003) identified the ASD severity of the child with ASD (as measured by the Autism Behavior Checklist; Krug, Arick, & Almond, 1980) as a predictor of sibling total behaviour problems (as measured by the Strengths and Difficulties Questionnaire; Goodman, 1997). Similarly, Petalas et al. (2012) reported that the ASD severity (as measured by the Autism Spectrum Quotient; Baron-Cohen et al., 2006), as well as the total behavioural problems of the child with ASD affected the total behavioural problems of the sibling. Kaminsky and Dewey (2002) found that siblings of children with ASD reported greater admiration and less competitiveness and conflict with their brother or sister than siblings of typically developing children.

Summary:

- Most research indicates that the behaviour of siblings of children with DS is no different to that of siblings of typically developing children.
- However, research into the behaviour of siblings of children with ASD yields mixed results.
- No differences were found when the siblings of children with ASD were compared with the siblings of children with DS.
- Age and gender (including whether the siblings are the same gender or not) affect sibling adjustment.
- Child behaviour problems and ASD symptom severity are both positively associated with sibling behaviour problems.

PART B: QUESTIONNAIRE SURVEY OF ENGLAND AND WALES

Chapter 6: Autism characteristics and behavioural disturbances in children with Down syndrome

Outline

- The key research questions for the questionnaire survey are outlined.
- The method is described, including participants, recruitment, response rates, outcome measures, statistical analyses and details of ethical approval.
- The characteristics of the survey sample and the findings of the survey are reported.
- Discussion of the survey findings is presented. For each research area a summary box of key findings is provided, followed by an interpretation of the findings in the context of previous research.

6.1 Introduction

Recent research shows that a substantial proportion of children with Down syndrome (DS) also meet diagnostic criteria for an autism spectrum disorder (ASD) (see Chapter 3). To date, studies that have utilised an autism specific screening tool to explore the rate of individuals with DS meeting threshold for ASD have been geographically localised, modest in size and have explored wide age ranges. The present survey is the first to assess the rates of autism characteristics in children with DS across England and Wales. Moreover, the survey aimed to validate previous reports of behavioural problems, communication disturbance and regression in children with DS who meet the threshold for ASD. The survey aimed to answer the following research questions:

1. What proportion of children (aged 6-15 years) with a confirmed diagnosis of DS in England and Wales meet cut-off scores for ASD (total score ≥15) and autism (total score ≥22) on the Social Communication Questionnaire (SCQ)?

2. How far can the survey data be used to estimate rates of ASD in children with Down syndrome?

3. What is the gender ratio of children who meet cut-off scores?

4. Do children with DS who meet the SCQ cut-off for ASD show a specific pattern of general behaviour problems compared with those who score well below cut-off (i.e. total SCQ score <10)?

5. Do children with DS who meet cut-off for ASD on the SCQ show greater communication problems compared with children who score well below cut-off?

6. Is the incidence of reported regression higher in the group who meet cut-off for ASD on the SCQ compared with those scoring below cut-off and when were signs of regression identified?

7. Have parents of children scoring above cut-off experienced particular problems with regard to finding appropriate educational placements for their child compared with parents of children who score well below cut-off?

6.2 Method

Section 6.2.1 Participants

Inclusion criteria

A survey pack was distributed to all members of the UK Down's Syndrome Association (DSA) with a child aged between 6 and 15 years who lived in England or Wales. These demographics were determined by the DSA records. Members who lived in Scotland or Northern Ireland were not included in the study due to time and cost restraints associated with visiting the families in the later stages of the project. The lower age limit was set at 6 years in order to avoid the inclusion of participants from a concurrent study investigating infants with DS and co-morbid ASD being carried out at the University of Newcastle. The upper age limit was set at 15 years so that consent to participate remained with the parents or carers of the child.

Consent

A survey pack entitled *'Differences among children with Down syndrome'* was sent to each member of the DSA who met the inclusion criteria. These were distributed by the DSA and personal details were not disclosed to the researchers at King's College London. An information sheet was included and completing and returning the questionnaires indicated consent to be involved in the survey study. A consent form to be contacted about

further research was also included in the pack which gave the participants space to provide contact details. (See Appendix B for information sheet and consent form)

Representativeness of the Down's Syndrome Association

According to the 'Annual Mid-year Population Estimates for England and Wales' (Office for National Statistics, 2012), the number of children aged 7-16 years[7] in 2012 was 6,437,298. Prevalence of DS in England and Wales in 2011 was estimated at 0.66 per 1000 people (Wu & Morris, 2013). Using these figures it can be estimated that there were around 4,249 children with DS within the age range in England and Wales. At the time of recruitment the DSA had 1,382 members in the given age range (i.e. approximately 33% of the total England and Wales DS population).

Section 6.2.2 Recruitment

The questionnaires were distributed either by post or by email. The preferred method of distribution was by email, to save paper, cost of postage and time inputting data. However, the DSA did not have email addresses for all of their members. For those whom they did (n=534), a link to an online survey was emailed along with a personalised username and a password. For those members for whom they did not have an email address (n=848), paper copies of the questionnaires were posted.

Copyright

In order to create online versions of the questionnaires (Social Communication Questionnaire and Strengths and Difficulties Questionnaire; see Section 6.2.4 for descriptions) permission was sought from the copyright owners. This was granted in both cases (see Appendix B for correspondence). The presentation of the questionnaires onscreen resembled the paper versions as far as possible, as changes in presentation can undermine the comparability of data.

Section 6.2.3 Response rate

Figure 6.1 outlines the response rate to the survey. Of the families contacted by post, around a third returned the survey pack. The response rate was marginally higher by email (see Figure 6.1). Eight responses had to be excluded as the child's age was either not given

[7] The age range of 7-16 years was used (opposed to 6-15 years) because the children were recruited in mid-2011 and the population estimates were produced for mid-2012. Therefore, the cohort of children represented in this study would have aged by 1 year.

or fell outside the inclusion criteria. Although the response rate appears quite low, it is recognised as a good response for the DS population. As a group, individuals with DS are heavily researched which results in a high level of demand on their time which can lead to a high level of non-participation (Moss et al., 2013b).

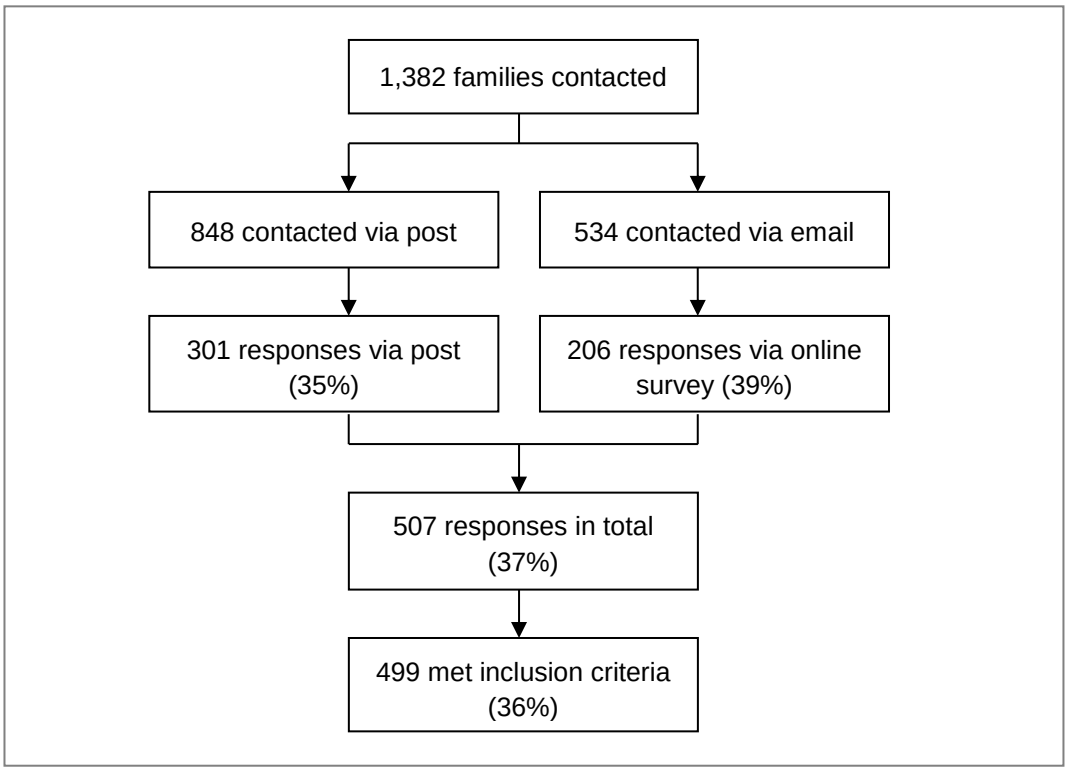

Figure 6.1 Response rates to the questionnaire survey

Section 6.2.4 Measures

Lifetime version of the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003)

The SCQ is a 40-item parent report screening measure that identifies characteristics associated with ASD. Each item is dichotomous and scored to indicate the presence (score=1) or absence (score=0) of the autism characteristic; severity of behaviour is not rated. A total score of 15 indicates ASD, and 22 autism. The items can be divided into 3 subdomains: Reciprocal Social Interaction, Communication, and Restricted, Repetitive and Stereotyped Patterns of Behaviour, and are deliberately matched to those on the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter & Couteur, 1994), a structured interview commonly used in clinical assessment of ASD. The 'lifetime' version of the SCQ refers to the entire developmental history of the child. Item level validity is good, with 31 out of 39 items significantly differentiating individuals with ASD from those

without (Berument et al., 1999; Bölte, Holtmann & Poustka, 2008). The recommended ASD cut-off of 15 has been found to differentiate between individuals with special educational needs with and without ASD with sensitivity and specificity rates of .86 and .78 respectively (Charman et al., 2007).

There are limitations to the use of the SCQ. It cannot be used to diagnose ASD because in order to do so information is required on the onset and possible context specificity of symptoms. Also, the instrument relies entirely on the perception of the parent and many items are based on personal judgement. Further to this, the screening instrument was designed with typically developing children in mind as the main comparison group. Impairments in social interaction and communication and/or the presence of repetitive and stereotypic behaviours are clear when considering the development of a child against typical developmental behaviour. However, certain autistic characteristics that are identified by the SCQ are also found in many other developmental disorders, including DS. Nevertheless, Magyar et al. (2012) conducted a psychometric evaluation of the SCQ in a sample of children with DS and concluded that the screening tool is suitable to use with this group. The measure was found to be reliable and to accurately categorise the children according to whether they had co-morbid ASD or not (Magyar et al., 2012).

Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997)

The SDQ is a screening measure for the psychological adjustment of children and young people. The questionnaire has 25 items rated on a 3-point Likert scale (Not True/Somewhat True/Certainly True). The 25 items are divided between 5 scales of 5 items each, generating scores for emotional symptoms, conduct problems, hyperactivity, peer problems and prosocial behaviour. A total difficulties score, ranging between 0 and 40, is generated by summing all of the subscores with the exception of prosocial behaviour. The SDQ version used for the current study was the extended parental report for 4 to 16 year old children. The extension to the questionnaire also includes a brief impact supplement that enquires further about overall distress, social impairment, burden and chronicity.

A study evaluating the psychometric properties of the SDQ (Goodman, 2001) concluded that the parent form had good internal consistency, with Cronbach α coefficients ranging from .57 to .85 across the subdomain, total and impact scores. Mean retest stability after an interval of 4-6 months was .63 but Goodman notes that this should in fact be taken as a *minimum estimate* as the period between the tests is too great and behaviours may have changed in this time, affecting the ratings given.

Although the SDQ is an excellent tool for screening for psychological adjustment in children, it does rely on the perception of the parent. Therefore, the results can only be taken as an indication of problem behaviours.

General Information Questionnaire

A general information questionnaire was created specifically for the present study in order to obtain further information about the development of the children. The questions covered the following topics: communication methods, regression in language and general skills, appropriateness of educational provision and experiences of seeking alternative provision, genetic source of DS, feelings of the child not fitting the 'typical' DS profile, seeking a further diagnosis, closest town or city and number of siblings. Some questions were based on the ADI-R. (See Appendix B for a copy of the questionnaire).

English Indices of Deprivation (Office for National Statistics, 2007)

Information from the English Indices of Deprivation Report (2007) was utilised in order to determine the socioeconomic status of the survey respondents. The report considered several factors, including income, employment, health, education, barriers to housing and services, living environment and crime. These elements were weighted and combined to form a deprivation index. The population weighted district level averages of deprivation were applied to the respondents. The report labelled each district in England according to the decile in which it scored. Each respondent was assigned a numerical value of 1 to 10 according to the district they lived in and the percentile in which that district fell (1=most deprived, 10=least deprived). For the purpose of evaluation, the deciles were grouped into the 'most deprived' (deciles 1, 2 and 3), the 'moderately deprived' (deciles 4, 5, 6 and 7) and 'least deprived' (deciles 8, 9 and 10). Respondents who did not specify their location with enough detail to be allocated to a specific district were excluded from this analysis (n=37). Respondents who resided in Wales (n=22) were also excluded as information on Welsh districts was not available.

Section 6.2.5 Statistical analysis

The Statistical Package for the Social Sciences (SPSS) Version 20.0 was used for data analysis. Data were entered into the database (accessed only by a password) using identification numbers to retain participant anonymity. Hard copies of the data were stored in a locked filing cabinet at the Institute of Psychiatry. All data were tested for normality using Kolmogorov-Smirnov tests and visual inspection of histograms. Homogeneity of

variance between the comparison groups (i.e. DS+ASD and DS-only) was tested using Levene's tests. If the data were normal and homogeneity of variance achieved parametric tests (e.g. t-tests) were utilised. However, if these assumptions were violated non-parametric tests (e.g. Mann Whitney U tests) were utilised. In the latter case, if homogeneity of variance was not achieved this was noted and findings interpreted cautiously as, although by virtue of ranking the data Mann Whitney U tests reduce the impact of outliers, there is still some suggestion that the underlying distributions should be similar in shape (Sheskin, 2003).When Mann Whitney U tests were used the standardised z statistic was reported. Chi-square tests were used to assess the association between categorical variables, with Fisher's exact statistic reported when ≥20% of the cells had an expected count less than 5.

A proportional SCQ Communication subscale score was derived for non-verbal children in order to ensure that general communication difficulties were comparable across the groups. Eaves et al. (2006) used a similar strategy. The proportional communication score was derived using the following calculation: (Sum of domain items completed / No. of domain items completed) x 13. The mean score was multiplied by 13 as there are 13 items in the communication domain. Although the majority of scores were unchanged or changed by less than 1 point (n=407), 78 (16%) were changed by more than 1 point. The greatest point difference was 5 (n=22).

Significance level

Data were examined for significance using a .05 p-value. Effect sizes (Pearson's r for t-tests, Cliff's d for Mann Whitney U tests, and Cramer's V for Chi-square tests (or Phi (φ) in the case of 2x2 tables) were also reported. Pearson's r is commonly used and widely accepted. It considers the strength of association and thus is arguably the most accurate type of effect size for continuous data (Ferguson, 2009), which the majority of measures in the present study produce. Cramer's V/Phi (φ) also considers the strength of association, but it useful in representing the effect size of categorical data and is commonly applied to Chi-square tests (Ferguson, 2009). Cliff's d has been put forward as an alternative to Pearson's r for non-parametric tests (e.g. Mann Whitney U tests); rather than estimating mean differences it measures the extent to which one distribution lies above another (Cliff, 1993). Effect sizes were interpreted according to Cohen's benchmarks of small=.10, medium=.30, and large=.50 (Field, 2005). Equations used to calculate effect sizes can be found in Appendix B.

Power analysis

A power analysis was conducted using nQuery Advisor 4.0 based on a reported ASD in DS frequency percentage of 15.6% (Lowenthal et al., 2010)[8] (see Section 3.1). Based on a 95% confidence level, 298 responses were reportedly needed in order to achieve a 4% confidence interval (CI) on the statistics produced in the present study, 530 responses to achieve a 3% CI, and 1,191 to achieve a 2% CI.

Missing data

With a survey of such scale, item non-responses were expected and strategies were put in place in order to handle such missing data. Parents were informed that they did not have to include any identifying information on the questionnaires. For some this meant that they did not include the requested information relating to the child's date of birth. Information about the age of the child was needed to ensure they met inclusion criteria; plus age was a variable in some statistical analyses. Therefore, those responses without any indication of the child's date of birth (n=5) were dropped from the dataset. If the response included only year of birth (n=3) the 15th June was entered into the database i.e. the midpoint of the year.

SCQ scores were considered central to the study, as much of the categorisation of children for analyses was based on these scores. Any ambiguous responses (for example if the parent/carer had answered both 'yes' and 'no' to a question) were treated as missing data. As long as 75% or more items were completed a replacement method was adopted, whereby missing values were replaced with the mean score for that child on a subscale level. If the amount of missing data exceeded this cut-off the SCQ data were excluded from analysis. This is a recognised method of dealing with missing data on the SCQ (Moss et al., 2013b).

A similar strategy was adopted for missing or ambiguous data on the SDQ. Ambiguous responses were treated as missing. Missing values were replaced with the mean score for that child on a subscale level if at least 75% of the items in that subscale were completed. Otherwise, the SDQ data were excluded from analysis.

Missing answers on the General Information Questionnaire could not be treated in this way and if questions were not completed then that child was simply excluded from any analyses that utilised the information from those questions.

[8] The figure from the Lowenthal et al. (2010) study was used in the power analysis because it was a large scale study which utilised the same method as the current study (i.e. SCQ data only, cut-off=15). DiGuiseppi et al. (2010) reported weighted figures based on several measures. The Moss et al. (2013b) paper was not available at the time of conducting the power analysis.

Defining comparison groups

For comparative analyses, children who met the ASD cut-off (total SCQ score ≥15) were referred to as the DS+ASD group (n=183); children who scored well below cut-off on the SCQ (total score <10) were referred to as the DS-only group (n=190). A total score of 10 was taken as the lower cut point as it lies below the basal score that has been identified as useful in the detection of ASD (cut-off=11, Eaves, Wingert, & Ho, 2006) . Furthermore, Magyar et al. (2012) reported a mean SCQ total score of 9.13 for a DS only group. Although this sampling strategy should have provided a group representative of children with DS only, it must be noted that type II errors were still possible given the imperfect sensitivity rates of the SCQ.

Section 6.2.6 Ethical approval

Ethical approval for the survey was granted to Professor Patricia Howlin by the Psychiatry, Nursing & Midwifery (PNM) Research Ethics Subcommittee in January 2011 (Project Reference: PNM/10/11-4). Ethical approval was also granted to Georgina Warner for subsequent modifications to the project by the PNM Research Ethics Subcommittee in September 2011. (see Appendix B)

6.3 Characteristics of the survey sample

Age and gender

Figure 6.2 illustrates the age distribution of the sample. The dates of birth of 5 children were missing and 3 children fell outside the age criteria. These 8 children were excluded from all analyses. The age appropriate sample consisted of 499 children, 281 male (56%) and 218 female (44%).

Genetic mechanism of Down syndrome

Of the parents who knew the nature of their child's genetic mutation (n=460), 95% (n=437) of children had Trisomy 21, 3% (n=12) Mosaicism and 2% (n=11) Translocation.

Verbal ability

According to parental reports on the General Information Questionnaire, 76.0% (n=377) of the sample were able to use phrase/sentence speech, 15.3% (n=76) communicated using only single words and 8.7% (n=43) were non-verbal[9].

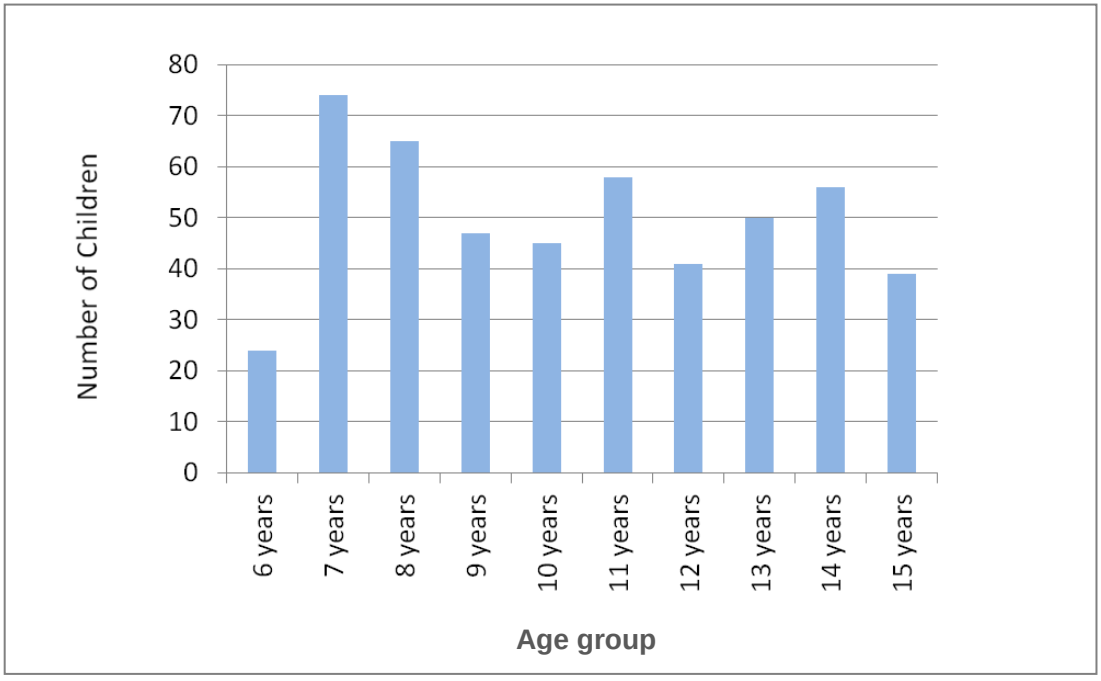

Figure 6.2 Age distribution of the sample (total n=499)

[9] Three responses to this question were missing

Geographical spread of sample

Figure 6.3 illustrates the geographical spread of the survey respondents around England and Wales. Each marker represents a location of response, *not* an individual respondent. In many cases there were several respondents from one location. For example, cities such as Birmingham and Leeds had numerous respondents, as well as smaller locations such as Truro in Cornwall. Respondents who did not specify their location with adequate detail were excluded from this graphical presentation (n=37). The geographical spread of respondents covered most regions of England and Wales. However, clusters were evident in the London and Manchester areas. Furthermore, there were few respondents from the Lincolnshire area and Welsh locations are quite sparse.

Socioeconomic status of sample

Figure 6.4 describes the socioeconomic status of respondents who resided in England (n=440) as measured by the English Indices of Deprivation (see Section 6.2.4). The data show that the sample was evenly distributed in terms of socioeconomic status when the deciles were grouped to form the most deprived (deciles 1, 2 and 3; 36%), the moderately deprived (deciles 4, 5, 6 and 7; 32%) and least deprived (deciles 8, 9 and 10; 32%)[10].

[10] Fifty-nine families were excluded from this analysis (see p.63 for details)

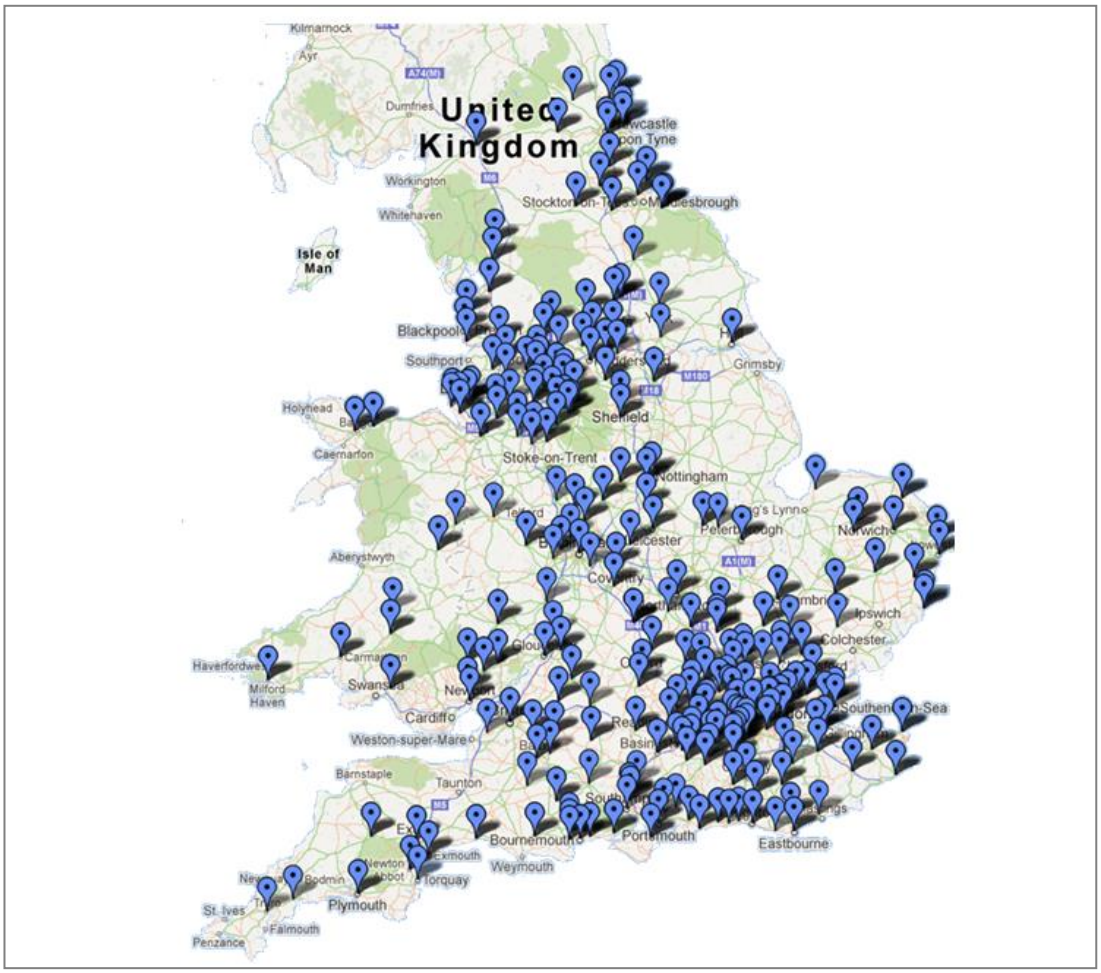

Figure 6.3 Geographical spread of survey respondents

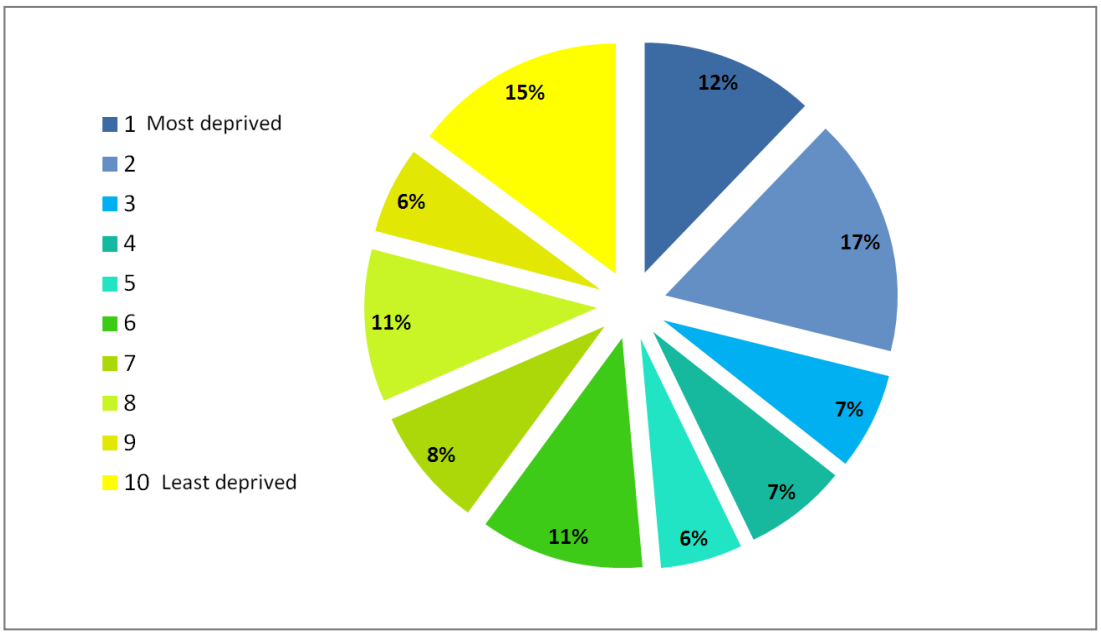

Figure 6.4 Distribution of sample across the deciles of deprivation

6.4 Results

Section 6.4.1 Proportion of children with Down syndrome and autistic characteristics

Research question 1: What proportion of children (aged 6-15 years) with a confirmed diagnosis of DS in England and Wales meet cut-off scores for ASD (total score ≥15) and autism (total score ≥22) on the SCQ?

The proportion of children with DS who met the recommended cut-off score for ASD (≥15) was 37.7% (95% confidence interval [CI]: 33.4% - 42.0%). The proportion of children who met the recommended cut-off score for autism (≥22) was 16.5% (95% CI: 13.2% - 19.8%) (Figure 6.5)[11]

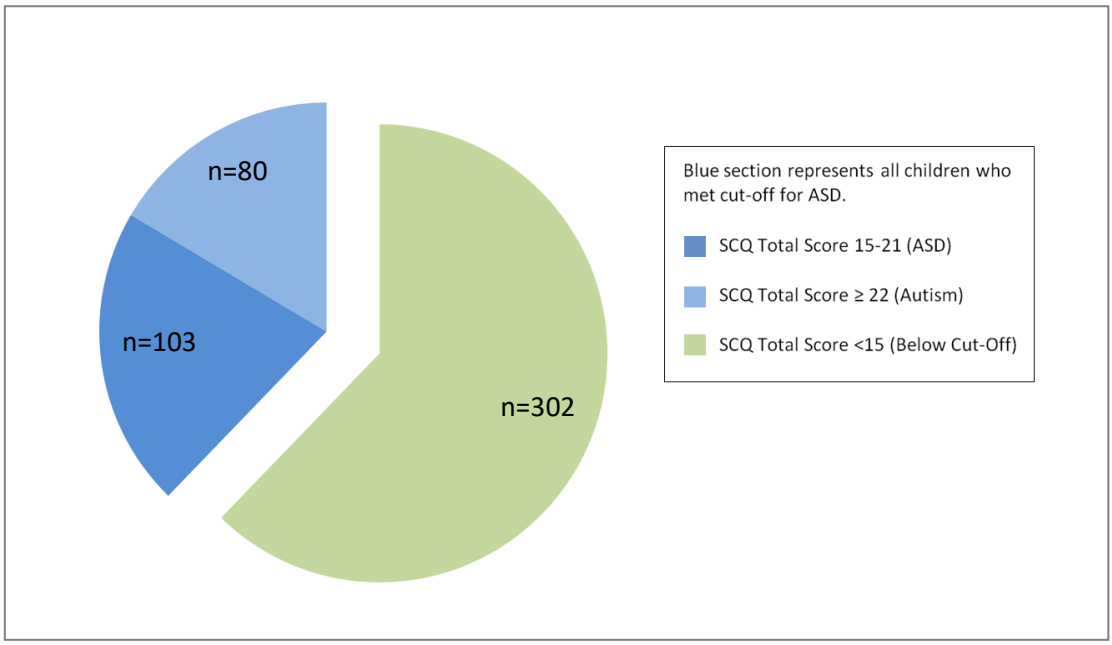

Figure 6.5 Proportion of children with DS who met cut-off scores for ASD and autism on the SCQ

[11] Total n=485; 14 SCQ forms were not fully completed

Section 6.4.2 Epidemiological model

Research question 2: How far can the survey data be used to estimate rates of ASD in children with Down syndrome?

It is important to note that the reported proportions cannot be interpreted as prevalence figures as this was not an epidemiological study (see Section 6.6.3 for further details). A model was built upon government birth statistics and previous research findings to produce an estimated prevalence of ASD in children with DS in England and Wales (see Figure 6.6).

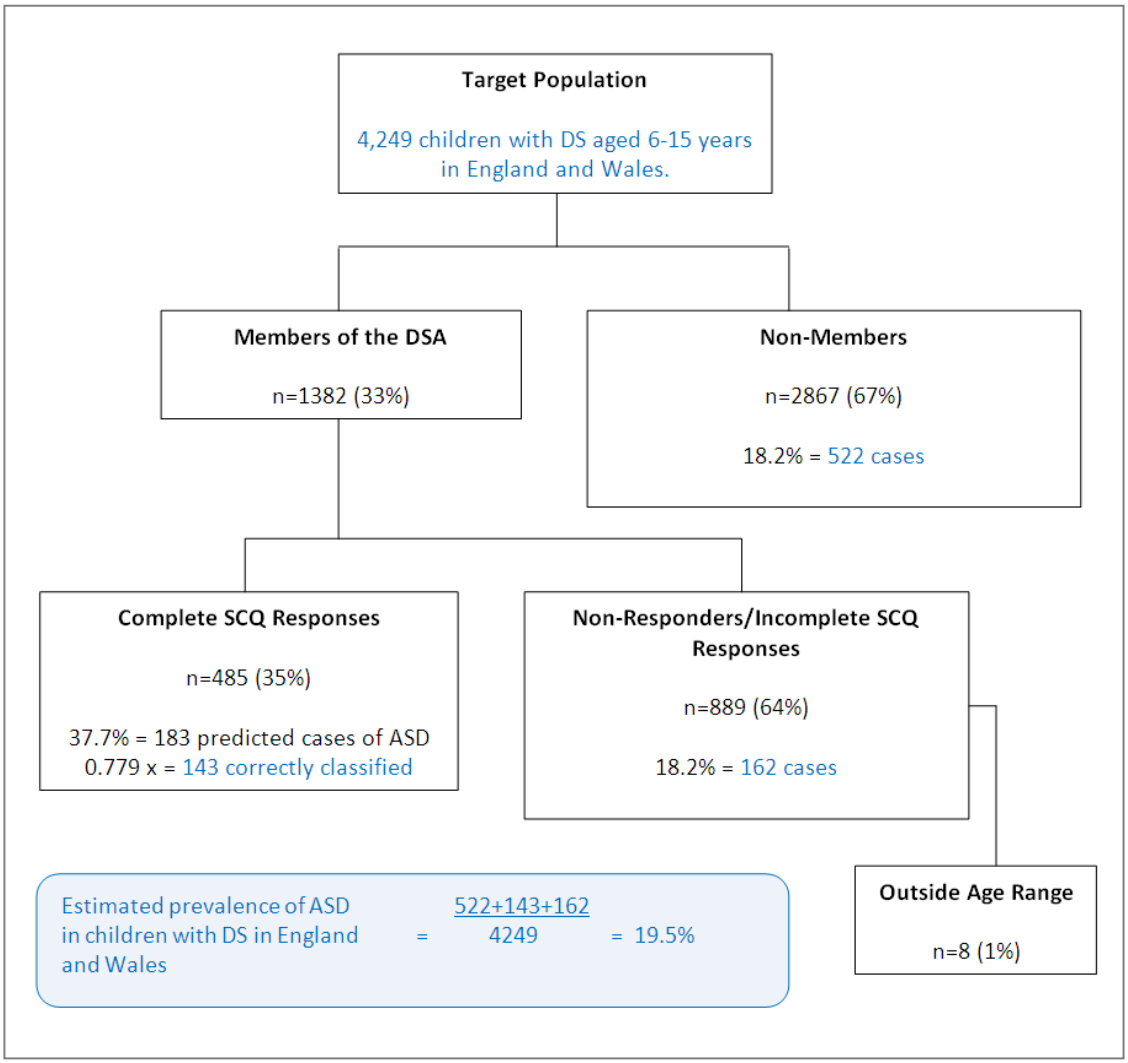

Figure 6.6 Epidemiological model of the prevalence of ASD in children with DS aged 6-15 years in England and Wales

Section 6.4.3 Gender ratio

Research question 3: What is the gender ratio of children who meet cut-off scores?

Of the children who scored at or above the cut-off for ASD on the SCQ (n=183), 123 (67%) were male and 60 (33%) were female. Among those scoring at or above the autism cut-off (n=80) 60 (75%) were male and 20 (25%) were female (see Figure 6.7).

There was a significant association between gender and meeting the ASD cut-off on the SCQ (≥15), χ^2 (1, N=485) = 14.26, **p<.001**, φ=.17. Males were more likely to score at or above this cut-off (OR=2.05). There was also a significant association between gender and the higher cut-off score for autism (≥22), χ^2 (1, N=485) =13.63, **p<.001**, φ=.17, with males, again, being more likely to score at this level (OR=2.69).

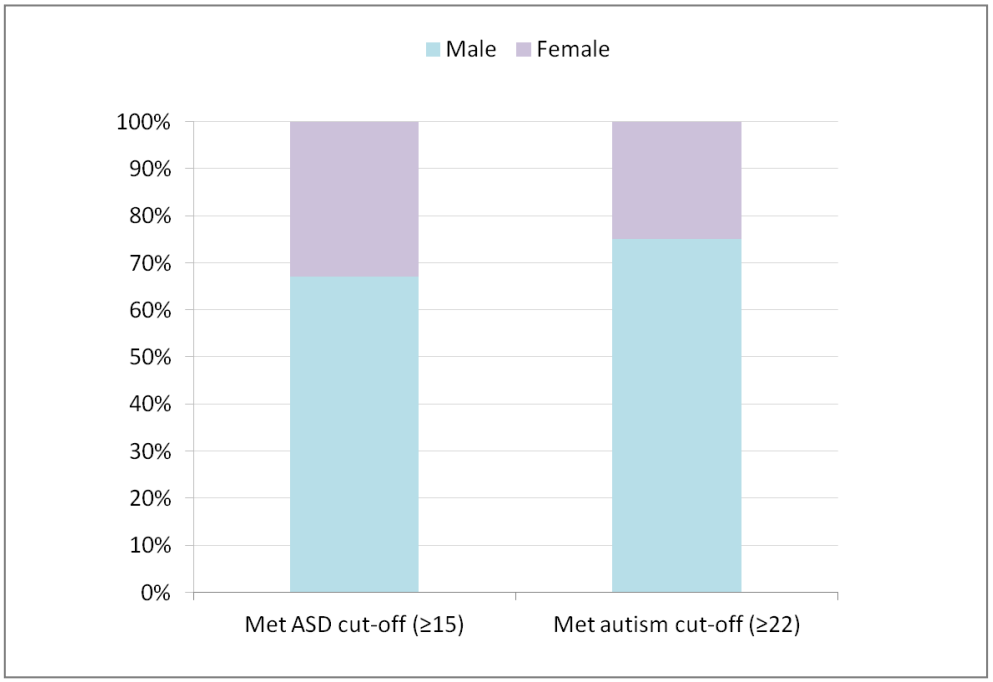

Figure 6.7 Gender distributions of children meeting cut-off scores on the SCQ

Section 6.4.4 Characteristics of the subsamples

Table 6.1 outlines the characteristics of the subsamples used for comparative analyses (see p.70 for further details on classification of comparison groups). The DS+ASD group were marginally older and had slightly more males (albeit with small effect sizes). The DS+ASD group scored significantly higher on the SCQ.

Table 6.1 Age, gender and SCQ total scores for the DS+ASD and DS-only subsamples

		DS+ASD	DS-only	Group difference
N		183	189	
Age (years)	Mean (SD) Range	10.87 (2.78) 6.00-15.00	10.10 (2.80) 6.00 -15.00	t(370)=-2.66, **p<.05**, r=.14
Gender	% Male (N)	67.21 (123)	47.62 (90)	χ^2 = 14.59, **p<.001**, φ=.20
SCQ score	Mean (SD) Range	21.33 (5.34) 15.00-36.00	5.89 (2.44) 0.00-9.00	t(252.77)=-35.69, **p<.001**,r=.88

Section 6.4.5 Pattern of general behaviour problems

Research question 4: Do children with DS who meet the SCQ cut-off for ASD show a specific pattern of general behaviour problems compared with those who score well below cut-off?

Responses to the SDQ were compared between the DS-only group (SCQ <10) and the DS+ASD group (SCQ ≥15) at full scale and subscale level (emotional symptoms, conduct problems, hyperactivity, peer problems and prosocial behaviour)[12].

Children in the DS+ASD group were reported to show higher levels of general behaviour problems, Mann Whitney z=10.72, **p<.001**, Cliff's d=.65 (DS+ASD: median=17.00, inter-quartile range (IQR) =13.00-21.00; DS-only: median=10.00, IQR=7.25-13.00). Moreover, children in the DS+ASD group scored significantly higher, on average, than the DS-only group on *all* of the subscales except the prosocial behaviour scale, on which the DS-only group scored higher (see Table 6.2).

[12] Missing data: full scale (n=5), emotional symptoms (n=4), conduct problems (n=3), hyperactivity (n=3), peer problems (n=4), prosocial behaviour (n=3).

Table 6.2 Average scores of DS-only and DS+ASD children on the SDQ subdomains, and group differences

SDQ subscale[a]	**Group**	**Median**	**IQR**	**Mann-Whitney z**	**p**	**Cliff's d**
Emotional symptoms	DS only	1	0-3			
(Normative mean =1.9)	DS+ASD	3	1-4	5.48	**<.001**	.33
Conduct problems	DS only	2	1-3			
(Normative mean =1.6)	DS+ASD	3	2-4	5.96	**<.001**	.35
Hyperactivity	DS only	4	3-6			
(Normative mean =3.5)	DS+ASD	7	5-9	8.15	**<.001**	.49
Peer problems	DS only	2	1-4			
(Normative mean =1.5)	DS+ASD	5	3-6	9.59[b]	**<.001**	.57
Prosocial behaviour	DS only	8	7-9			
(Normative mean =8.6)	DS+ASD	5	3-7	-10.64[b]	**<.001**	.64

[a] Mean scores for normative sample (age 5-15 years) in parenthesis
[b] Conclusions to be treated with caution as the homogeneity of variance assumption has been violated

Section 6.4.6 Communication problems

Research question 5: Do children with DS who meet cut-off for ASD on the SCQ show greater communication problems compared with children who score well below cut-off?

Verbal ability

According to parental reports on the General Information Questionnaire (GIQ), over half of the children in the DS+ASD group were able to use phrase/sentence speech, around a fifth communicated using only single words and a similar proportion were non-verbal. Among those children in the DS-only group the majority were able to use phrase/sentence speech, and only 1% were non-verbal (see Table 6.3)[13].

There was a significant relationship between meeting cut-off on the SCQ and the ability to use phrase/sentence speech as measured by the GIQ, χ^2 (1, N=370) =52.67, **p<.001**, φ=.38. Children in the DS+ASD group were significantly less likely to speak using sentences and phrases, than children in the DS-only group (OR=0.6).

Children in the DS+ASD group scored significantly higher on the SCQ Communication domain than those children in the DS-only group, Mann Whitney z=15.08, **p<.001**, Cliff's d=.90 (see Figure 6.8)[14].

Age of language acquisition for verbal children

For children in the DS-only group, the median reported age of language acquisition was 28.0 months (IQR=20.5-36.0). It was 36.0 months (IQR=24.0-48.0) for those in the DS+ASD group, Mann-Whitney z=3.98, **p<.001**, φ=.26[15].

Table 6.3 Verbal ability of DS-only vs. DS+ASD children

Verbal Ability	Group	n (%)
Phrase/Sentence Speech	DS only	169 (90%)
	DS+ASD	103 (57%)
Single Words Only	DS only	17 (9%)
	DS+ASD	42 (23%)
Non-verbal	DS only	2 (1%)
	DS+ASD	37 (20%)

[13] Three responses to this question were missing
[14] Adjusted communication scores reported (please see Section 5.2.5 for further details)
[15] Sixty-five responses to this question were missing – mostly due to the question not being applicable to non-verbal children (Remaining group sizes: DS-only n=172; DS+ASD n=136)

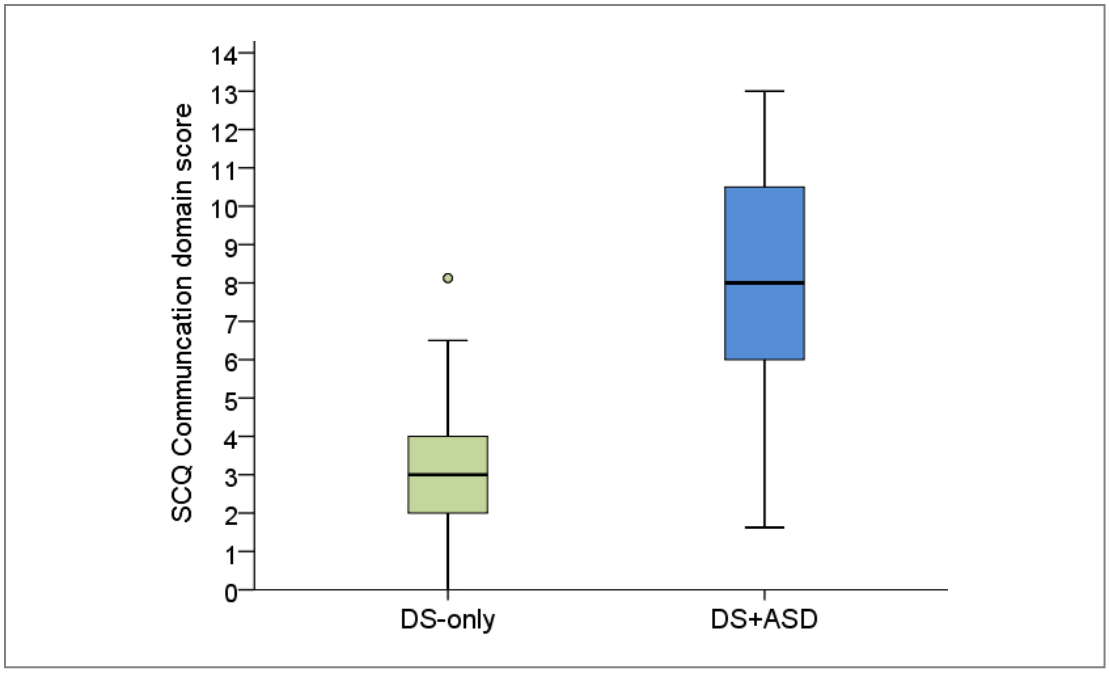

Figure 6.8 SCQ Communication domain scores for the DS-only and DS+ASD groups

Section 6.4.7 Regression in skills

Research question 6: Is the incidence of reported regression higher in the group who meet cut-off for ASD on the SCQ compared with those scoring below cut-off and when were signs of regression identified?

Reported regression in language skills

The percentage of parents who had been concerned that their child had lost language skills was lowest in the DS-only group. Over a third of children in the DS+ASD group were reported to show a regression in language skills. (Within the DS+ASD group, those who met the cut-off for autism (≥22) nearly half of parents reported regression) (see Figure 6.9)[16].

There was a significant relationship between meeting the SCQ cut-off score for ASD and a reported loss in language skills, χ^2 (1, N=363) =42.61, **p<.001**, φ=.34. Thus, children in the DS+ASD group were more likely to experience a reported loss in language skills than those children in the DS-only group (OR=4.5).

[16] Nine responses to this question were missing

Age of regression in language skills

For children in the DS-only group who had experienced a loss in language skills, the median reported age of loss was 33.0 months (IQR=23.0-72.0). For those in the DS+ASD group it was 36.0 months (IQR=23.0-60.0), Mann Whitney z=.14, p=.89, Cliff's d=.02.

Reported regression in general skills

A similar pattern of reported incidence emerged in relation to general skills (see Figure 6.10)[17]. There was a significant relationship between meeting the SCQ cut-off score for ASD and a reported loss in general skills, χ^2 (1, N=362) =40.57, **p<.001**, φ=.33. Thus, children in the DS+ASD group were more likely to experience a reported loss in general skills than children in the DS-only group (OR=4.8).

Age of regression in general skills

For children in the DS-only group who had experienced a loss in general skills, the median reported age of loss was 24.0 months (IQR=19.5-36.0). For those in the DS+ASD group it was 36.0 months (IQR=12.0-60.0), Mann Whitney z=.75, p=.45, Cliff's d=.15.

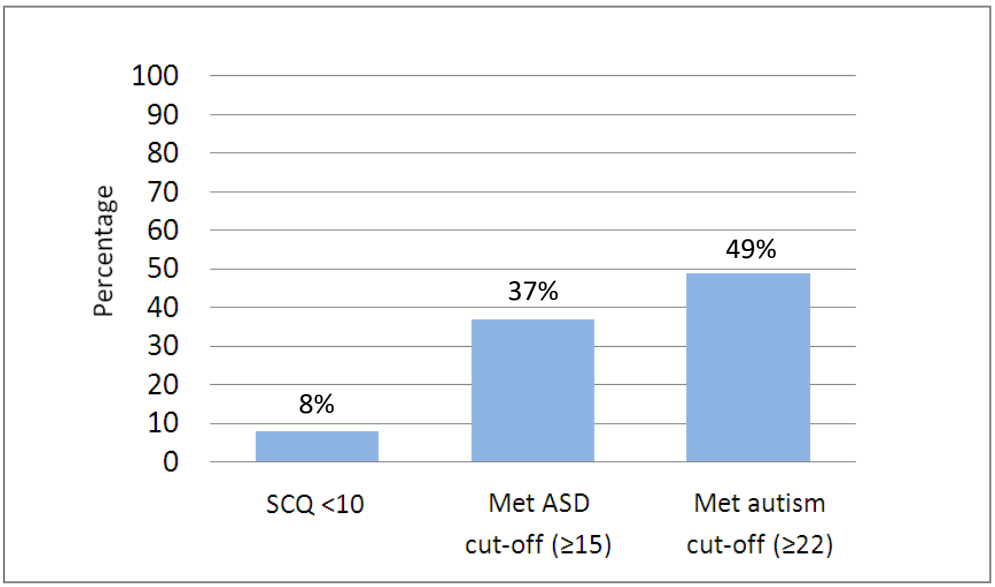

Figure 6.9 Reported loss of language skills according to SCQ cut-off scores

[17] Eleven responses to this question were missing

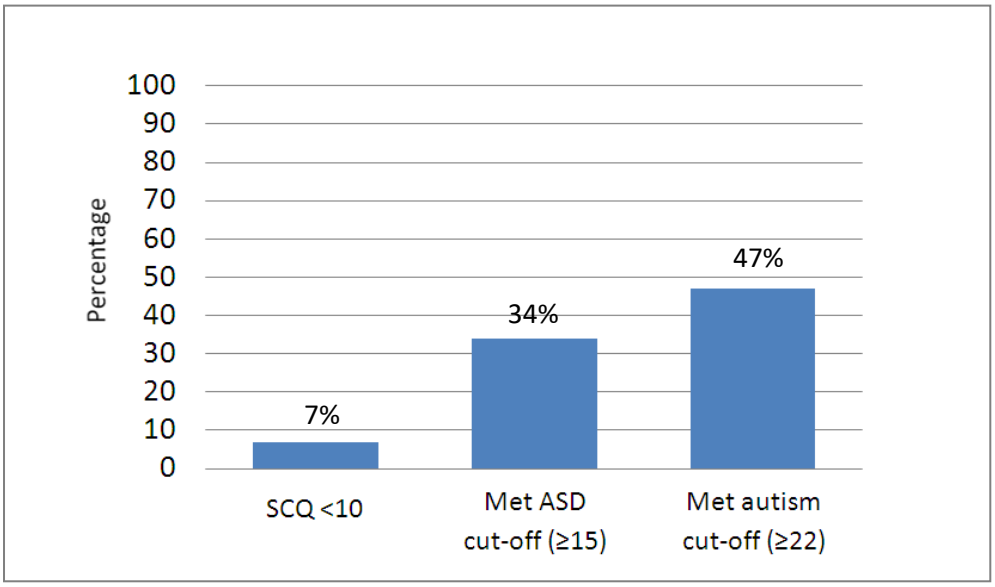

Figure 6.10 Reported loss of general skills according to SCQ cut-off scores

Section 6.4.8 Appropriateness of educational placements

Research question 7: Have parents of children scoring above cut-off experienced particular problems with regard to finding appropriate educational placements for their child compared with parents of children who score well below cut-off?

A greater proportion (21.0%) of the parents with a child in the DS+ASD group reported that their child's educational provision was inappropriate, compared with parents of children in the DS-only group (12.5%), χ^2 (1, N=360) =4.71, **p<.05**, φ=.11.
Thus, parents were more likely to have considered their child's educational provision as inappropriate if their child met the cut-off score for ASD (OR=1.7)[18].

Similarly, a greater proportion (37.3%) of the parents with a child in the DS+ASD group had sought alternative education than parents of children in the DS-only group (20.0%), χ^2 (1, N=362) =13.28, **p<.001**, φ=.19. Thus, parents were more likely to have sought alternative educational provision if their child met the cut-off score for ASD (OR=1.9)[19].

[18] Thirteen responses to this question were missing
[19] Eleven responses to this question were missing

6.5 Further analyses

Section 6.5.1 Clinical diagnoses of autism spectrum disorder

Seeking a diagnosis

Eighty-three (45%) parents with a child in the DS+ASD group had sought a clinical diagnosis of ASD/autism. Of those families, 50 (60%) were successful in attaining an ASD or autism diagnosis. Twelve (15%) cases were still under review at the time of the survey, and 21 (25%) were informed that their child was not on the autistic spectrum or an assessment was not given.

Experience of seeking a diagnosis

The nature of comments made by respondents about seeking a diagnosis was assessed. Comments were coded according to whether they were *positive*, *negative* or *neutral*. Codes were assigned by two independent raters (kappa = .90; $p<.001$). The majority of respondents who had been given a diagnosis of ASD or autism and the majority of respondents who were being assessed at the time of the survey gave *neutral* comments about the diagnostic process. However, the majority of respondents who had not been given a diagnosis of ASD or autism gave *negative* comments about the process (see Table 6.4). Examples include:

"Our paediatrician is old school - all I get told is 'that's Down's for you'."

"I have asked repeatedly for him to be assessed for autism but always told children with Down's syndrome can have similar traits to children with autism."

"I feel from a professional view that our child has a lot of autistic tendencies and I have tried to get a diagnosis but with no luck."

"Very difficult – folk don't want to get too involved"

Table 6.4 Nature of comments about seeking a diagnosis

Diagnostic status	n	Comments		
			Rater A (Rater B)	%
Diagnosis given	50	Positive	4 (3)	8
		Negative	9 (10)	18
		Neutral	37 (37)	74
Diagnosis *not* given	21	Positive	0 (0)	0
		Negative	13 (14)	62
		Neutral	8 (7)	38
Pending	12	Positive	0 (0)	0
		Negative	4 (3)	33
		Neutral	8 (9)	67

Percentages based on the outcome of Rater A (GW)

Socioeconomic status related to diagnosis

Respondents who had sought a diagnosis of ASD/autism were fairly evenly distributed in terms of socioeconomic status according to government deprivation scores (see Section 6.2.4, p.67) (most deprived=36%; moderately deprived=24%; least deprived=40%)[20]. Of those who had sought a diagnosis, socioeconomic status did not appear to be related to whether or not a diagnosis was given (see Table 6.5). However, it appeared as though the majority of respondents waiting to hear the outcome of an assessment were in the least deprived group.

Table 6.5 Socioeconomic statuses of parents who have sought a diagnosis of ASD/autism

Diagnostic status	N	Socioeconomic status
Diagnosis given	50	40% Most Deprived 20% Moderately Deprived 40% Least Deprived
Diagnosis *not* given	21	28% Most Deprived 50% Moderately Deprived 22% Least Deprived
Pending	12	27% Most Deprived 9% Moderately Deprived 64% Least Deprived

[20] Deprivation scores were not assigned to 7 respondents (see Section 6.2.4, p.67 for possible reasons)

Section 6.5.2 Speech and language therapy provision

Respondents were given an opportunity to elaborate on their experiences of seeking alternative educational provision. This was an open-ended question and no specific provision was listed on the questionnaire form (see Appendix B for the General Information Questionnaire). One issue that emerged was that respondents were unhappy with the extent of Speech and Language Therapy (SLT) provided. Of the 485 respondents who completed this section of the survey, 44 (9%) elected to write that they felt the need to provide additional SLT for their child as these needs were not being met.

6.6 Discussion

Section 6.6.1 Characteristics of the sample

The characteristics of the sample were evaluated in order to gauge the representativeness of the DS population as a whole. The particular characteristics investigated were: age, gender, genetic mechanism of DS, verbal ability, geographical spread, and socioeconomic status.

Age

There seemed to be an underrepresentation of 6 year olds in the sample, accompanied by a greater than expected proportion of 7 and 8 year olds. This may be due to the fact that the differences between children with DS and their peers become increasingly more evident with age. This is reflected in school placements; the proportion of children with DS who attend a mainstream school in the UK decreases as child age increases (Buckley & Bird, 2000). As parents become more aware of the cognitive, linguistic and social differences between their child with DS and other children they tend to become more involved in support groups and this could account for the increased level of 7 and 8 year olds in the present study.

Gender

Although males were marginally overrepresented, the gender distribution of the sample was fairly even at 56% male, 44% female which is comparable with the general DS population. The importance of achieving an even gender distribution in the current study was twofold. First, gender is central to research question 2 (*what is the gender ratio of children who meet cut-off scores?*). An overrepresentation of a gender in the DS sample

may be resultant in an overrepresentation in the screen positive group (i.e. the DS+ASD group), which could be a product of sampling bias rather than a true indication of the gender ratio of the co-morbidity. Second, female gender has been related to lower cognitive ability in ASD (Rivet & Matson, 2011). Therefore, a misrepresentation of gender may have had a secondary effect on the cognitive ability of the samples.

Genetic mechanism

The proportions of children within the sample with each genetic source of DS were as expected and thus representative of the wider population (see Chapter 1, Section 1.4).

Verbal ability

The verbal ability of the sample is consistent with previous samples. Reports on the General Information Questionnaire indicated that 91.3% of the children were verbal. Moss et al. (2013b) report 93.5% of their participants as being verbal. This high proportion of children with vocal language is consistent with reports that, although communication development is often delayed and may be impaired, most children with DS will become vocal language users in the course of the first 3 years of life (Abbeduto, Warren & Conners, 2007).

Geographical spread

The geographical spread of respondents was fairly evenly distributed across England and Wales. Although clusters (as well as areas of greater sparsity) were evident, the current sample was far more representative geographically than previous studies, which have adopted cluster sampling of localised areas (e.g. DiGuiseppi et al., 2010; Lowenthal et al., 2010; Moss et al., 2013b). There is some suggestion that there may be geographical variation in the prevalence of ASD (Scott et al., 2002). The national scale of the present survey overcomes possible sampling bias related to geographical location.

Socioeconomic status

When the data regarding the socioeconomic status of the respondents (as measured by the English Indices of Deprivation) were grouped to form the ‘most deprived’, the ‘moderately deprived’, and the ‘least deprived’, the sample was evenly spread indicating that the respondents were representative of all social classes. Although no association has been

found between socioeconomic status and risk of ASD (Larsson et al., 2005), it is important to continue to be aware of socioeconomic status in studies of this kind.

Characteristics of the subsamples

Very similar proportions of the total DS survey sample fell into the DS+ASD (38%) and DS-only (39%) groups. Although this did not result in precisely equal groups, it would have improved comparability. The DS+ASD group were marginally older than the DS-only group; however, the effect size of the difference was small. Therefore, age was not considered as a covariant in comparative analyses (research questions 4-7). The DS+ASD group had a slightly higher proportion of males; despite suggestion that higher male prevalence found in ASD is lacking in the DS population (Lowenthal et al., 2007), this group characteristic was not surprising given the overrepresentation of males in idiopathic ASD (Fombonne, 2003). Due to the characteristic being an acknowledged clinical feature (coupled with a small effect size of group difference), gender was not considered as a covariant in comparative analyses. Moreover, the type of analyses used prohibited the use of age and/or gender as covariates; Chi square analyses were conducted for categorical data and Mann-Whitney U tests for continuous data (as the data were found to be skewed).

Section 6.6.2 Proportion of children with Down syndrome and autistic characteristics

- The proportions of children with DS who met the cut-offs for ASD and autism on the SCQ were 37.7% (n=183) and 16.5% (n=80) respectively.

These figures are clearly elevated when compared with previous figures generated by the same screening tool (15%, Lowenthal et al., 2010; 19%, Moss et al., 2013b) and there are several possible reasons for this. First, the questionnaire packs were entitled ‘Differences among children with Down syndrome’. The purpose of this was to avoid worrying parents unnecessarily about the possible presence of ASD in their children. However, it is likely that families who had identified their child as somewhat ‘different’ to the stereotypical perception of DS were more likely to respond as they personally identified with the title of the study. Second, despite recent publication dates, data collection for the previous studies cited above was carried out around 2005-2006. Survey data for the present study was collected in 2011. Knowledge and understanding of the co-morbidity has developed rapidly over the last decade and parents in the present survey may have been more aware

than parents in earlier studies of ASD characteristics in their children. Third, the present sample was at least twice the size of previous studies and increased statistical power means that the findings are more likely to be representative.

There are, of course, limitations regarding the sampling strategy of the present study (i.e. recruiting through the Down's Syndrome Association (DSA)), as this may have led to bias in the findings. Internal analyses by associations such as the DSA identify that they do not reach all demographics within the population, for example ethnic minorities tend to be underrepresented. However, this does not explain the higher rates identified in the present study, as Moss et al. (2013b) also recruited through the DSA. It should be noted though that Moss et al. (2013b) recruited only from the London and Birmingham areas; it may be the case that this circumscribed geographical location affected the demographics of the sample.

Section 6.6.3 Epidemiological model

- Estimated prevalence of ASD in children with DS (aged 6-15 years) in England and Wales was 19.5%.

It is important to note that the proportions of children meeting cut-off scores on the SCQ cannot be interpreted as prevalence figures. This was *not* an epidemiological study in that participants were recruited through the Down's Syndrome Association (DSA) rather than through a centralised register for DS, since no such register exists in the UK.

The findings may also be affected by sampling bias. Parent associations, such as the DSA, generally tend to include higher proportions of middle class and/or better educated individuals than typical of the general population. Moreover, families who are members of the DSA may be more in need of support than those who are not. In addition, given that the survey was entitled *'Differences among children with Down syndrome',* those who responded to the survey may have been more likely to be experiencing difficulties than those who did not and/or were more likely to view their child as being different from the 'typical' DS child.

The epidemiological model (Figure 6.6) estimated the target population and applied a previously reported prevalence statistic of ASD in DS (18.2%) to all non-members of the DSA and non-responders. The rate of 18.2% was taken from the DiGuiseppi et al. (2010) paper. It was selected because that study recruited via a birth defects register rather than a

support group. In addition, a diagnostic accuracy figure for the SCQ (0.779; Magyar et al., 2012) was applied to the screen positive cases from the current survey. This accuracy figure was not applied to the non-members and non-responders because DiGuiseppi et al. (2010) had already corrected for the accuracy of the screening tools utilised in their study.

There are clear limitations to the model. First, an assumption was made about the size of the target population; the number of children with DS in the age range was calculated using government population estimates and a reported DS prevalence figure (see Section 6.2.1, p.64). Second, the prevalence rate applied to the non-members and non-responders was selected from a small body of research. Moreover, the DiGuiseppi et al. (2010) study was based in North America; therefore, the direct application of the rate to children in England and Wales could be questioned. However, it is important to recognise the original limitations of the sampling strategy adopted in the present research and to work towards providing a more accurate rate of ASD in children with DS in England and Wales, hence the formation of the model.

Section 6.6.4 Gender ratio

- The proportion of males meeting the ASD cut-off on the SCQ was significantly greater than the proportion of females.

This finding is *not* consistent with previous gender ratios produced by the SCQ in this population. Although a greater proportion of males met the ASD cut-off in the studies conducted by Lowenthal et al. (2007; OR=1.6)[21] and Moss et al. (2013b; OR=1.6), neither of these findings were significant. A higher proportion of males (as found in the current study) is consistent with trends seen in idiopathic ASD, where a male to female ratio of 4:1 is typical (Fombonne, 2003). It may be that the sample sizes of the studies have affected the outcomes. The gender difference found in the present study (2:1), although significant, is less pronounced than that seen in idiopathic ASD. The implication of this result is ambiguous; it could be that DS in some way protects males from the risk of ASD, or it could amplify the risk in females.

[21]The Lowenthal et al. (2007) publication is referenced because the Lowenthal et al. (2010) publication does not provide details on gender.

Section 6.6.5 Pattern of general behaviour problems

Compared with children with DS only, children in the DS+ASD group:

- were reported to show significantly more emotional symptoms, conduct problems, hyperactivity and peer problems
- were reported to show significantly less prosocial behaviour

An increased level of hyperactivity is a consistent finding that differentiates individuals with DS and co-morbid ASD from individuals with DS only (Capone et al., 2005; Carter et al., 2007; Dressler et al., 2011; Ji et al., 2011; Moss et al., 2013b). The present study adds to this body of research, indicating that hyperactivity is common to the behavioural phenotype of DS and co-morbid ASD.

The presence of conduct problems appears to be a more variable finding, sometimes reported as more common in this group (compared to DS individuals without ASD) (Ji et al., 2011) and sometimes not (Hepburn & Maclean, 2009). Parent reports from this study suggest that the level of conduct problems is raised in children who met threshold for ASD. It may be that there is individual variability in disruptive behaviour amongst children with DS and co-morbid ASD. Or, given that each of the studies utilised a different questionnaire, different constructs of problem behaviour have been measured.

Some items that contribute to the SDQ emotional symptoms scale refer to the child being worried, nervous, clingy and scared; therefore, the higher level of emotional symptoms reported for children with DS+ASD could be compared with previous reports of increased anxiety in this group (Carter et al., 2007). However, heightened levels of anxiety within DS and co-morbid ASD is not a consistent finding; Dressler et al. (2011) and Hepburn and Maclean (2009) reported no difference between DS and co-morbid ASD and DS only groups on measures of anxiety.

Section 6.6.6 Communication problems

- When compared with the DS-only group, the DS+ASD group showed poorer general communication skills and were less likely to use verbal communication.
- Of those who did have language, children in the DS+ASD group acquired their first words at a later age than children in the DS-only group.

The deficits in communication are consistent with previous research noting poorer receptive and expressive language in children with DS/Trisomy 21 and co-morbid ASD (Dressler et al., 2011; Magyar et al., 2012; Molloy et al., 2009).

Section 6.6.7 Regression in skills

- Children in the DS+ASD group were significantly more likely to be reported as showing a loss in both language skills and general skills than children in the DS-only group.
- However, the average age at which regression was reported did not differ between the groups.

Castillo et al. (2008) reported significant differences in the age of regression in general skills between children with idiopathic ASD and children with DS and co-morbid ASD, with the latter group showing the decline at a later age (19.5 months vs. 46.2 months). The present study could *not* replicate this finding because a DS/DS+ASD comparison was made. However, a similar mean age of reported regression in general skills for the DS+ASD group was produced (41.2 months)[22]. The mean age of regression in the Castillo et al. (2008) idiopathic ASD group is similar to that reported in a previous paper (24 months; Davidovitch et al., 2000). These collective findings are suggestive of the developmental regression common to idiopathic ASD also being present in children with DS and co-morbid ASD, but the occurrence is somewhat delayed. This could be linked to the delayed acquisition of language reported in DS (Abbeduto et al., 2007)[23].

However, the age of regression in language in the present study was notably lower than in the Castillo et al. (2008) paper (45.3 months vs. 61.8 months). This difference could be due to the small sample size in the Castillo et al. (2008) study, in which only 6 DS+ASD cases showed definite language loss, compared to the present study in which 66 children in the DS+ASD group were reported to have lost language skills.

[22] Median ages are reported in the results chapter (36.0 months for both regression in language skills and regression in general skills).
[23] Note that a difference was seen in the age of language acquisition in the present study (DS+ASD later than DS-only), albeit with a small effect size.

Section 6.6.8 Appropriateness of educational placements

- Parents of children in the DS+ASD group were significantly more likely to describe their child's educational provision as inappropriate and report seeking alternative provision.

There is a tendency in the UK for children with DS to attend mainstream primary education initially and then to transfer to a special school placement at secondary level. These placements are usually at schools for children with severe learning difficulties ('SLD' schools) or schools for children with moderate learning difficulties ('MLD' schools) (Buckley & Bird, 2000). In contrast, children with a diagnosis of ASD have the option, from nursery onwards, of attending an ASD-specific school. They may also have access to autism-specific teaching programs. For example, the Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH; Mesibov, Shea & Schopler, 2004) programme has been widely adopted in the UK.

Children in the DS+ASD group may be better suited to the environment of an ASD specific school. However, as many of the children in the DS+ASD group do not have an ASD diagnosis (see Section 6.5.1), it is less likely for them to be accepted in ASD-specific provision. This may be why parents of children in the DS+ASD group were more likely to describe their child's educational provision as inappropriate and report seeking alternative provision.

Section 6.6.9 Further analyses

Clinical diagnoses of autism spectrum disorder

Less than half of the parents of children in the DS+ASD group had sought a clinical diagnosis of ASD/autism. This may be due to the lack of awareness and understanding of the co-occurrence of the disorders among parents. Although research into the co-morbidity has been published in academic journals in recent years (see Chapter 3), dissemination to the parent population may have been limited.

The majority of parents who had been unsuccessful in attaining a diagnosis made negative comment about the process. A few examples of these comments touched upon the age of the clinician and lack of enthusiasm to pursue the diagnostic process. It may be the case that some clinicians are still following the views presented in their early training which would have indicated that DS rarely co-occurs with ASD (Rutter & Hersov, 1985).

Furthermore, as the children will have received the diagnosis of DS at birth, and the ASD diagnosis would be *an addition* to an existing diagnosis, some clinicians may view the ASD diagnosis as less important or relevant than might be the case for a child without other obvious impairments.

Speech and language therapy provision

The views noted on speech and language therapy (SLT) are consistent with the views of SLT clinicians, who are also concerned with having too little time for direct therapy and the time that is required to complete administrative duties (Pring et al., 2012). This may be associated with the recent government cuts to NHS funding, which have affected SLT clinical practice (The RCSLT Cuts Survey, 2012).

6.7 Limitations

There are a number of limitations associated with this survey that restrict the conclusions that can be drawn. Firstly, all the data were attained through informant measures and there was no direct assessment of the children themselves. Such reliance on parent reports created the opportunity for misinterpretation of items. Direct assessment of the children (e.g. administration of the Autism Diagnostic Observation Schedule-Generic [ADOS-G; Lord et al., 2000] and/or the Autism Diagnostic Interview-Revised [ADI-R; Rutter, LeCouteur & Lord, 2003]) would have provided more valid measures of ASD characteristics, allowing for more robust groupings and a more effective analysis of the autism profile. However, the selected measures are of a high standard; the SCQ has been reported in previous studies as having good convergent validity with ASD diagnostic assessments, specifically when used with individuals with DS (Magyar et al., 2012) and the SDQ has good internal consistency and is widely used in clinical settings. Moreover, time and resources did not permit the direct assessment of such a large sample.

Secondly, this cannot be considered as an epidemiological study as participant families were volunteers recruited through the Down's Syndrome Association. Moreover there is no way of knowing whether there were differences between survey responders and non-responders. However, the demographics of the sample were evenly spread and therefore representative of the wider population in terms of gender and socioeconomic status. Furthermore, the proportions of participants with each genetic mechanism of DS reflected those of the DS population (Freeman, 2007). Although fairly low, the response

rate of 36% exceeded that of previous studies (DiGuiseppi et al., 2010; Moss et al., 2013b) and this is the largest sample size in a study of this kind. More general limitations of the study are discussed in Chapter 12, Section 12.2.

6.8 Conclusions

Using the largest sample to date, this study identified the proportions of children with DS meeting cut-off scores for ASD and autism on the SCQ to be 37.7% and 16.5% respectively. These figures are much higher than those reported in previous studies, probably due to differences in sampling methods and sample characteristics. Children who met the ASD threshold were reported to have higher levels of emotional symptoms, conduct problems, hyperactivity and communication difficulties than individuals with DS only. Reports of regression, in both general and language skills, were also more common for this group. These findings provide support for previous reports that suggest individuals with DS and ASD have a distinct phenotypic presentation. Further, more detailed investigation using direct assessment and observational measures is required to gain a better understanding of the difficulties and needs of children with both DS and co-morbid ASD.

Chapter 7: Autism characteristics and behavioural disturbances: a comparison of data from the questionnaire survey with data from samples with idiopathic ASD

Outline:
This chapter describes a study comparing data on the DS+ASD group from the questionnaire survey (see Chapter 6) with two idiopathic ASD groups. Autism profiles were compared using data from the Social Communication Questionnaire and behavioural disturbances compared using data from the Strengths and Difficulties Questionnaire. The method, results, discussion, limitations and conclusions are presented.

7.1 Introduction

The comparison of children with Down syndrome (DS) and co-morbid autism spectrum disorder (ASD) with children who have DS only is important given that the recognition and diagnosis of the co-morbidity requires clarification of the differences between these 2 groups. However, co-morbidity can result in subtle differences in the phenotypic presentation of disorders. Thus, it is important to clarify the distinct autism profile of children with DS, and to assess whether the behavioural difficulties of children with DS and co-morbid ASD are comparable with children with ASD only, in order to advise parents and educators of appropriate interventions. To date, very few studies have made comparisons between individuals with DS and co-morbid ASD and individuals with idiopathic ASD (Castillo et al., 2008; Dressler et al., 2011; Moss et al., 2013b), and existing research has been conducted with very small sample sizes ($n \leq 17$ per group). This is the first study to conduct a large scale analysis of autism profiles across DS-only / DS+ASD / ASD-only groups and to compare the behavioural disturbances of children with DS and co-morbid ASD with those of children with idiopathic ASD. The study aimed to answer the following research questions:

1. Among children with DS who meet the cut-off for ASD on the SCQ, and those who score well below cut-off, how does the profile of ASD characteristics differ from that of individuals with idiopathic ASD?

2. Do children with DS who meet the SCQ cut-off for ASD show a specific pattern of general behaviour problems compared with children with idiopathic ASD?

7.2 Method

Section 7.2.1 Participants and measures

The comparison of Social Communication Questionnaire (SCQ) data with the reference percentages contained in the SCQ manual is an established method for assessing the autism profile of individuals with a genetic disorder and co-morbid ASD (see Hall et al., 2010 for an analysis of Fragile X syndrome). Thus, the DS+ASD group from the initial survey (see Chapter 6, Section 6.2.5, p.70 for details on categorisation and Tables 6.1 or 7.1 for group characteristics) were compared with the group used to establish the diagnostic validity of the SCQ (Berument et al., 1999). A concurrent study being conducted by the Pan-London Autism School Network-Research (PLASN-R) project also provided SCQ data, enabling the analysis to be repeated with an age-matched group. Outcomes on the Strengths and Difficulties Questionnaire (SDQ) were also compared with the age-matched group. It should be noted here that although effort was made to find an age-matched group, comparability between the groups might have been affected by ability level. The PLASN-R group were matched for verbal ability (see below), although this was by means of a dichotomous question on the SCQ and not a detailed measure of verbal ability. It is likely that the DS children were of a lower cognitive ability than the idiopathic ASD groups, which could have resulted in skewed findings. Unfortunately, IQ data were not available for any of the groups. Even if IQ data were available, the nature of the analyses (odds ratios and Mann Whitney U tests) would not have allowed for this covariate to be controlled. For details on the SCQ and SDQ see Chapter 6, Section 6.2.4. Missing data for the PLASN-R group were treated according to the methods outline in Chapter 6, Section 6.2.5 (p.69).

SCQ manual reference group

The reference group included 160 individuals with Pervasive Developmental Disorder (PDD) aged 4 to 40 years. The group had a high proportion of males (80%). All of the individuals had previously been assessed on the Autism Diagnostic Interview (original and/or revised). Eighty-three met criteria for autism; the remaining 77 were classified as ‘other PDD’.

Pan-London Autism School Network group

PLASN-R is a network of researchers and special schools for children with ASD in the London area which was formed to improve knowledge sharing across educational research and practice (Parsons et al., 2013). The schools provide valuable input into research design as well as offering a research setting and participants. Research is focussed around school issues, and research outcomes are applied to school practice.

A subsample of children matching the age range of the current study (i.e. 6-15 years) was selected from the PLASN-R database. The characteristics of the subsample, and group differences with the DS+ASD subsample, are reported in Table 6.1. The DS+ASD and PLASN-R groups were matched for age and verbal ability (according to the verbal screening item on the SCQ). There was a higher proportion of males in the PLASN-R group than the DS+ASD group (82.6% vs. 67.0%) and the PLASN-R ASD group also had a higher average score on the SCQ (24.2 vs. 21.3). This has implications for the comparability of the group. However, a less pronounced gender ratio appears to be a clinical feature of DS and co-morbid ASD (see Section 6.6.4). Moreover, the nature of the analyses did not allow for these factors to be controlled for.

Table 7.1 Age, gender, verbal ability and SCQ total score for the DS+ASD and PLASN-R groups

		DS+ASD	PLASN-R	**Group difference**
N		183	184	
Age (years)	Mean (SD)	10.87 (2.78)	10.98 (2.70)	t(365)=-.36, p=.72, r=.02
	Range	6.00-15.00	6.00-15.00	
Gender	% male (N)	67.21 (123)	82.61 (152)	χ^2 = 11.58, **p<.005**, φ=.18
Verbal ability	% verbal[a]	64.48 (118)	71.20 (131)	χ^2 =1.90, p=.17, φ=.07
SCQ score	Mean (SD)	21.33 (5.34)	24.22 (7.20)	t(337.63)=-4.36, **p<.001**, r=.23
	Range	15.00-36.00	4.00-39.00	

[a] '*Able to talk using short phrases or sentences'* according to SCQ (Q1)

Section 7.2.2 Statistical analysis

Analysis of autism profiles

Odds ratios were calculated to determine SCQ item-specific differences between the DS+ASD and DS-only groups and the ASD reference group (Hall et al., 2010; Moss et al., 2013a). The number of children in each group who scored on an individual SCQ item, and thus displayed the 'autism characteristic', was used to calculate odds ratios. An odds ratio

significantly more than 1 (i.e. outside the 99% confidence interval for that item) was taken to indicate that the autism characteristic was significantly more likely to be present in the DS+ASD (or DS-only) group rather than the ASD reference group. An odds ratio significantly less than 1 was taken to indicate that the autism characteristic was significantly less likely to be present in the DS+ASD (or DS-only) group rather than the ASD reference group. A second odds ratio analysis excluding non-verbal children was run for the 'social chat' item on the communication domain as this item, unlike others at the beginning of the form, was not subject to verbal ability screening.

Analysis of behaviour problems

All data were tested for normality using Kolmogorov-Smirnov tests and visual inspection of histograms. Homogeneity of variance between the comparison groups (i.e. DS+ASD and PLASN-R ASD) was tested using Levene's tests. If the data were normal and homogeneity of variance achieved parametric tests (e.g. t-tests) were utilised. However, if these assumptions were violated non-parametric tests (e.g. Mann Whitney U tests) were utilised. In the latter case, if homogeneity of variance was not achieved this was noted and findings interpreted cautiously as, although by virtue of ranking the data Mann Whitney U tests reduce the impact of outliers, there is still some suggestion that the underlying distributions should be similar in shape (Sheskin, 2003). When Mann Whitney U tests were used the standardised z statistic was reported.

Significance level

For the odds ratio analysis, items were taken to be significant if the value of 1 lay outside the 99% confidence interval for that item (Hall et al., 2010). For the comparison of behaviour problems, data were examined for significance using a .05 p-value. Effect sizes (Pearson's r for t-tests, Cliff's d for Mann Whitney U tests) were also reported. Effect sizes were interpreted according to Cohen's benchmarks of small=.10, medium=.30, and large=.50 (Field, 2005). (See Chapter 6, Section 6.2.5, p.68 for justification of the choice of effect sizes and Appendix B for effect size equations).

7.3 Results

Section 7.3.1 Autism profile compared with SCQ manual data

Research question 1: Among children with DS who meet the cut-off for ASD on the SCQ, and those who score well below cut-off (total score <10), how does the profile of ASD characteristics differ from that of individuals with idiopathic ASD?

Communication domain

Three impairments associated with ASD identified by items in the Communication domain of the SCQ were significantly more likely to be present in the DS+ASD group than the ASD reference group (see Figure 7.1). Children in the DS+ASD group were significantly *more* likely to be impaired on the following items: pronoun reversal (OR=4.5), using neologisms (OR=2.2), and social chat (OR=10.7). Conversely, children in the DS+ASD group were *less* likely to be impaired than the ASD reference group on imitation (OR=0.3), the use of gestures (OR=0.5), and imitative social play (OR=0.3).

The DS-only group were significantly *less* likely to be impaired than the ASD reference group on most items in the Communication domain. However, similar proportions of parents in the DS-only and ASD reference groups reported the use of neologisms (OR=1.0), and an impairment in social chat (OR=0.9). The DS-only group were significantly *more* likely to be impaired than the ASD reference group in reversing pronouns (OR=1.8).

Reciprocal Social Interaction domain

Six items in the Reciprocal Social Interaction (RSI) domain were significantly less likely to be present in the DS+ASD group than the ASD reference group (see Figure 7.2). Children in the DS+ASD group were significantly *less* likely to be impaired on the following items: eye gaze (OR=0.5); social smiling (OR=0.5); shared enjoyment (OR=0.5); offering comfort (OR=0.3); social overtures (OR=0.5) and response to other children's approaches (OR=0.4). No social interaction deficits, as measured by the SCQ items, were found to be statistically more likely to be present in the DS+ASD group than the ASD reference group.

The DS-only group were significantly *less* likely to be impaired than the ASD reference group on *all* items in the RSI domain (inappropriate facial expressions OR=0.2;

use of other's body OR=0.3; friends OR=0.1; imaginative play with peers OR=0.1). The odds ratios for the remaining items were all less than 0.1, except social smiling for which an odds ratio could not be calculated as *none* of the children in the DS-only group showed impairment in this area.

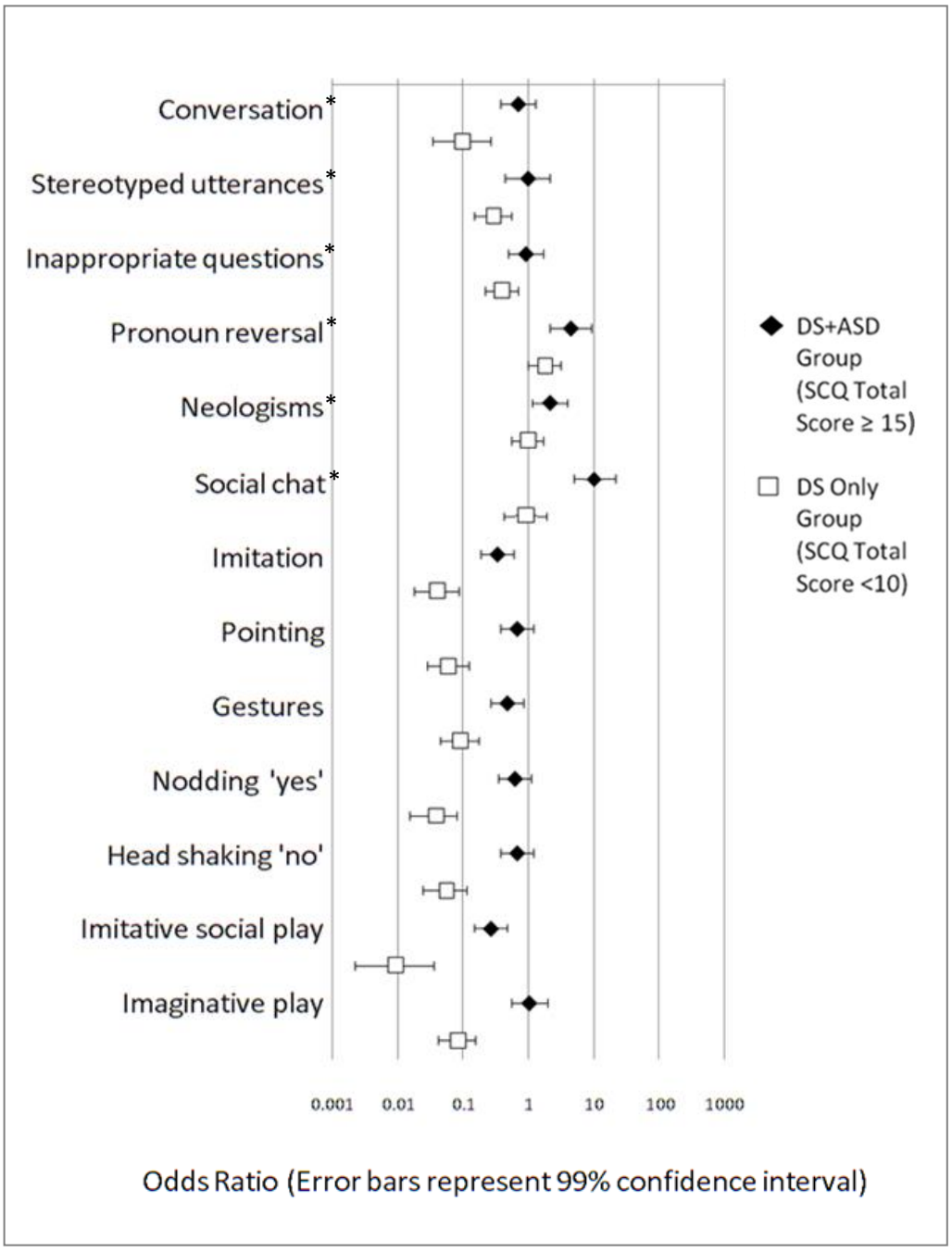

Figure 7.1 SCQ odds ratio analysis of Communication items

*verbal children only

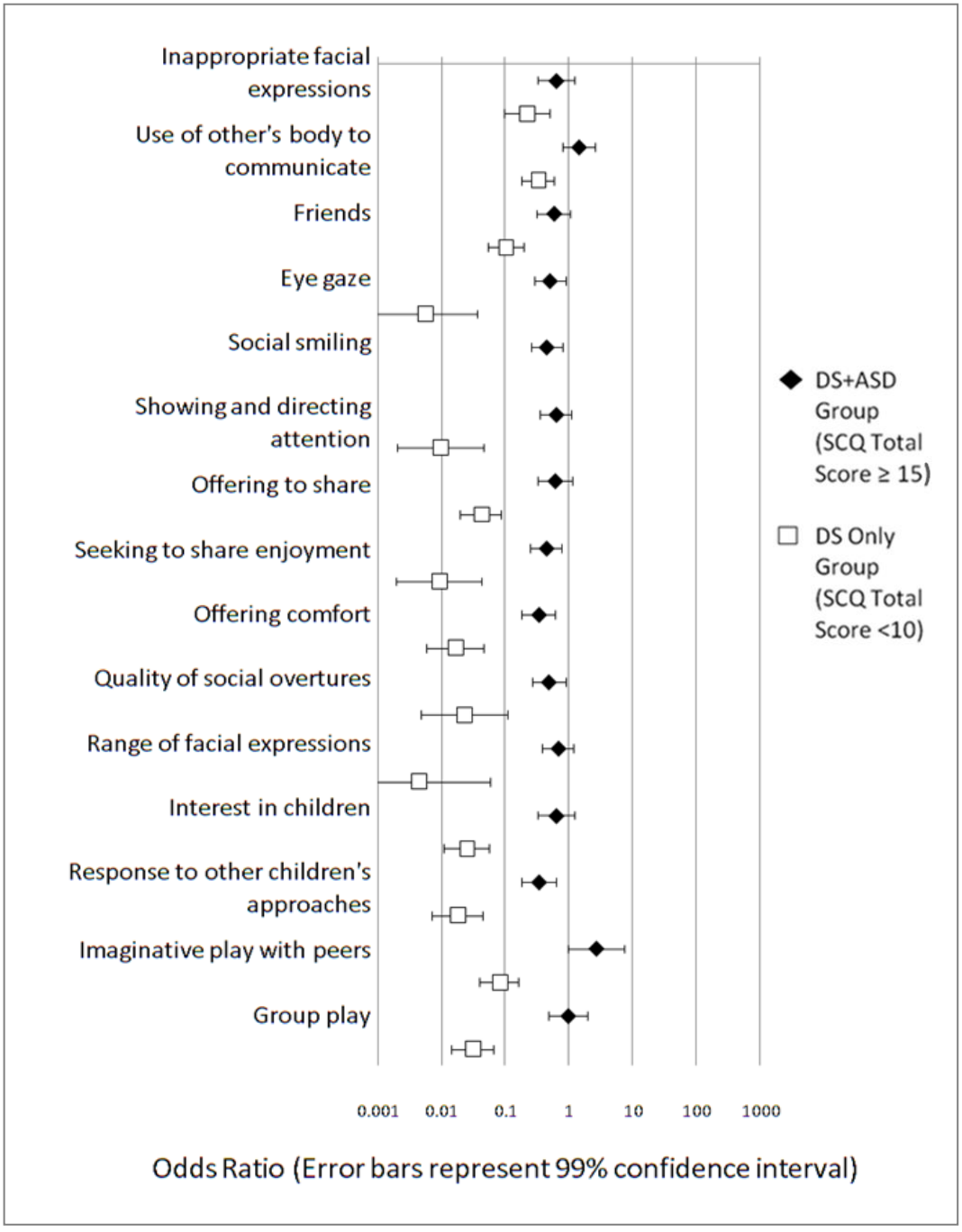

Figure 7.2 SCQ odds ratio analysis of RSI items

Restricted, Repetitive and Stereotyped Patterns of Behaviour domain

Only 1 item (compulsions and rituals) in the Restricted, Repetitive and Stereotyped Patterns of Behaviour (RRSPB) domain significantly distinguished between the DS+ASD group and ASD reference group (OR =2.9; see Figure 7.3). No SCQ items in this domain were found to be statistically *less* likely to be present in the DS+ASD group than the ASD reference group.

The DS-only group were significantly *less* likely to be impaired than the ASD reference group on *all* items in the RRSPB domain (verbal rituals OR=0.1; compulsions and rituals OR=0.4; repetitive use of objects OR=0.1; circumscribed interests OR=0.2; unusual sensory interests OR=0.1; complex body mannerisms OR=0.1). The odds ratios for the remaining items were less than 0.1.

Section 7.3.2 Autism profile compared with PLASN-R group

The verbal communication difficulties of the DS+ASD group identified in the first analysis were *not* apparent in the PLASN-R comparison; similar proportions of children in each group were impaired in pronoun reversal, use of neologisms and social chat (see Table 7.2). The relative strengths of the DS+ASD group in imitation and imitative social play remained; however, the group difference in the number of children using gestures ceased to be significant. The PLASN-R comparison produced similar differences in reciprocal social interaction profiles, with the DS+ASD group showing lower likelihood of impairment on many of the items (see Table 7.2 for slight differences). The comparison of restricted, repetitive and stereotyped behaviours produced the same outcome as the first analysis, with the DS+ASD group significantly more likely to have compulsions and rituals.

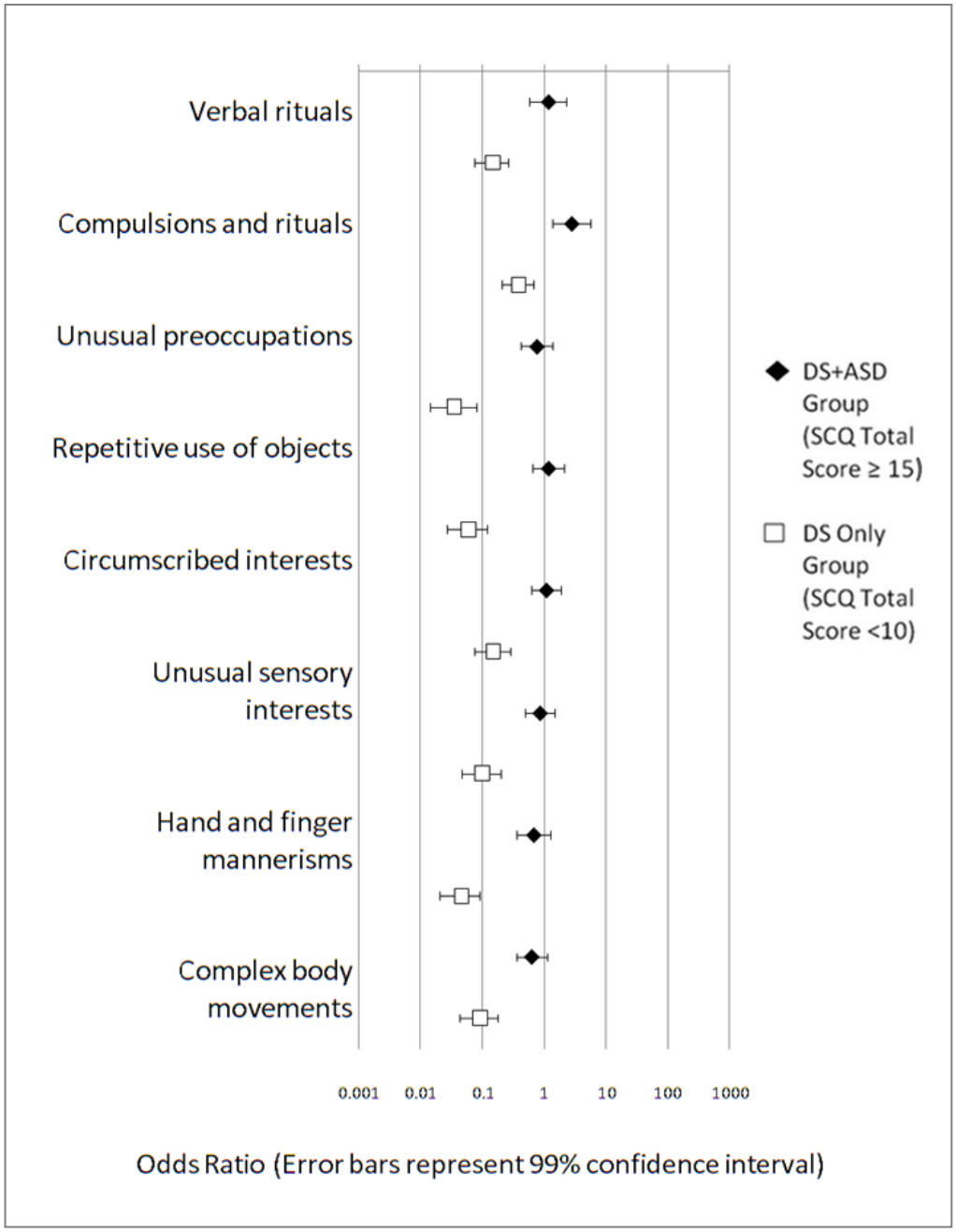

Figure 7.3 SCQ odds ratio analysis of RRSB items

Table 7.2 SCQ odds ratio analysis (DS+ASD vs. PLASN-R group)

	SCQ Item[a]	OR[a]	99% CI
Communication	Conversation	1.33	0.70-2.52
	Stereotyped utterances	0.85	0.49-1.46
	Inappropriate questions	1.03	0.59-1.80
	Pronoun reversal	**1.53**	0.89-2.64
	Neologisms	**1.10**	0.64-1.90
	Social chat	**0.99**	0.52-1.90
	Social chat (verbal only)	**0.71**	0.42-1.22
	Imitation	0.34*	0.19-0.59
	Pointing to express interest	0.99	0.58-1.71
	Gestures	**0.87**	0.51-1.49
	Nodding to mean 'yes'	1.06	0.61-1.83
	Head shaking to mean 'no'	0.95	0.55-1.64
	Imitative social play	0.24*	0.13-0.42
	Imaginative social play	0.80	0.43-1.52
Reciprocal Social Interaction	Inappropriate facial expressions	0.51*	0.27-0.95
	Use of other's body to communicate	1.04	0.58-1.87
	Friends	0.82	0.47-1.43
	Eye gaze	0.48*	0.28-0.84
	Social smiling	0.57*	0.33-0.99
	Showing and directing attention	1.15	0.67-1.97
	Offering to share	0.64	0.35-1.18
	Seeking to share enjoyment	**0.63**	0.37-1.10
	Offering comfort	0.45*	0.26-0.78
	Quality of social overtures	0.49*	0.27-0.88
	Range of facial expressions	**0.50***	0.29-0.86
	Interest in children	0.61	0.32-1.16
	Response to other children's approaches	0.46*	0.26-0.83
	Imaginative play with peers	1.65	0.56-4.83
	Group play	0.70	0.34-1.44
Restricted, Repetitive & Stereotyped Behaviour	Verbal rituals	1.03	0.60-1.77
	Compulsions and rituals	3.29*	1.66-6.52
	Unusual preoccupations	0.90	0.52-1.58
	Repetitive use of objects	0.94	0.52-1.70
	Circumscribed interests	0.91	0.52-1.56
	Unusual sensory interests	0.59	0.34-1.02
	Hand and finger mannerisms	0.89	0.50-1.61
	Complex body mannerisms	0.73	0.42-1.25

*****Significant (value of 1.00 lies outside the 99% confidence interval)

[a]Items in bold differ in significance from comparison with SCQ manual figures (see Section 7.3.1 and/or publication in Appendix A)

Section 7.3.3 Behaviour problems compared with PLASN-R group

Research question 2: Do children with DS who meet the SCQ cut-off for ASD show a specific pattern of general behaviour problems compared with children with idiopathic ASD?

Responses to the SDQ were compared between the DS+ASD group and the PLASN-R ASD group at full scale and subscale level (emotional symptoms, conduct problems, hyperactivity, peer problems and prosocial behaviour)[24].

A group difference was seen at full scale level, with the ASD group reportedly showing more behaviour problems (DS+ASD: median=17, inter-quartile range (IQR) =13-21; PLASN-R ASD: median=18, IQR=15-22), Mann Whitney z=2.40, **p<.05**, Cliff's d=.15. At subscale level, the ASD group were reported to show higher levels of emotional symptoms and peer problems than the DS+ASD group (see Table 7.3).

[24] Data were missing for 4 children in the DS+ASD group

Table 7.3 Average scores of DS+ASD and PLASN-R groups on the SDQ subdomains, and group differences

SDQ subscale[a]	Group	Median	IQR	Mann-Whitney z	p	Cliff's d
Emotional symptoms	DS+ASD	3	1-4			
(Normative mean =1.9)	PLASN-R	4	2-5	3.82	**<.001**	.23
Conduct problems	DS+ASD	3	2-4			
(Normative mean =1.6)	PLASN-R	2	1-4	-.62	.54	.04
Hyperactivity	DS+ASD	7	5-9			
(Normative mean =3.5)	PLASN-R	7	5-9	-.55	.59	.03
Peer problems	DS+ASD	5	3-6			
(Normative mean =1.5)	PLASN-R	5	4-7	3.35	**<.005**	.20
Prosocial behaviour	DS+ASD	5	3-7			
(Normative mean =8.6)	PLASN-R	4	2-6	-1.71	.09	.10

[a] Mean scores for normative sample (age 5-15 years) in parenthesis

7.4 Discussion

Main findings

Compared with an ASD reference group (SCQ manual) children in the DS+ASD group were more likely to demonstrate impairment in certain aspects of verbal communication and more likely to show compulsions or rituals. In contrast, they were less likely to show impairment in particular features of non-verbal communication and many aspects of reciprocal social interaction. Similar autism profile differences were seen in terms of reciprocal social interaction and restricted, repetitive and stereotyped behaviour when a second comparative analysis was conducted with an age-matched ASD group (PLASN-R). However, the relative deficits in verbal communication were no longer evident.

Similar levels of conduct problems, hyperactivity and prosocial behaviour were reported in the age-matched DS+ASD and ASD groups. However, the children in the DS+ASD group reportedly demonstrated fewer emotional symptoms than the children with ASD, and they experienced relatively fewer problems with peers.

Autism profile

The consistent finding that the DS+ASD group were less likely than the ASD groups to show impairment in imitation and imitative social play supports Dressler et al. (2011), who reported a significantly lower score on the Childhood Autism Rating Scales (CARS) imitation scale for a DS and co-morbid ASD group when compared with an idiopathic ASD group. Although categorised as a communicative trait by the authors of the SCQ, the reciprocal nature of imitation and imitative play gives the characteristics a 'social interaction' aspect. Indeed, the items loaded onto a 'social interaction' factor in a study evaluating the diagnostic validity of the SCQ (Berument et al., 1999). The relatively low level of impairment for these traits, and across many items in the reciprocal social interaction domain, in the DS-only and the DS+ASD groups suggests that the high level of social competence typically displayed by individuals with DS (Rosner et al., 2004) may act as a form of 'buffer' to the social deficits seen in ASD. Although a couple of differences were noted (i.e. *seeking to share enjoyment* ceased to be significantly lower in the DS+ASD group and *range of facial expressions* was identified as significantly lower in the DS+ASD group), reciprocal social interaction was recognised as an area of relative strength when the DS+ASD group were compared with the PLASN-R idiopathic ASD group.

The finding that verbal impairments in pronoun reversal, use of neologisms, and social chat were seen in the DS-only group as well as in the DS+ASD group implied that these communication deficits may be inherent in the DS phenotype. However, investigation into the expressive language profile of adolescents and young adults with DS found no difference in the use of personal pronouns when compared with a typically developing group (Finestack & Abbeduto, 2010). It is more surprising that there was no difference between the DS-only group and the ASD group in the reported rates of impairment in social chat (DS-only=19%; ASD=17%; DS+ASD=78%) given the characteristic differences in social competence between children with DS and those with autism more generally (Griffith et al., 2010). On further inspection of the data however, it seems that rate of impairment in the ASD reference group was unexpectedly low. Allison, Auyeung and Baron-Cohen (2012) found that a social chit-chat item on the Autism Spectrum Quotient Child Form (AQ; Baron-Cohen et al., 2001) was among the strongest items to discriminate between an ASD group and a control group, with a positive predictive value of .82. Therefore, one would expect a high level of impairment in a group of individuals with ASD. Furthermore, when the DS+ASD group were compared with an idiopathic ASD group provided by the PLASN-R project, no differences were seen on the pronoun reversal, neologisms or social chat items.

The increased rates of compulsions and rituals in the DS+ASD group are inconsistent with previous findings which have suggested that there are no significant differences between DS/DS+ASD groups in preoccupations and routines/rituals (Hepburn & Maclean, 2009) and no significant differences between DS/DS+ASD/ASD groups on compulsive behaviour, insistence on sameness or restricted preferences (Moss et al., 2013b). However, this may be due to differences in sample characteristics as the comparison groups in the Hepburn and Maclean (2009) study included young infants (age range 3-10 years). The Moss et al. (2013b) study included both infants and adults (age range 4-43 years) and the comparison groups were very small (n=17 per group). It may also be the case that the ability level of the DS children affected this finding. The groups were not matched for ability and it is likely that the DS children had a lower cognitive ability (given that the majority of individuals with DS have an IQ <70, whereas only approximately half of individuals with ASD have an IQ <70; see Chapters 1 and 2). Compulsions and rituals are common in individuals with low cognitive ability, which may account for the raised levels in the DS+ASD group compared with the idiopathic ASD group.

Behaviour problems

Although the level of emotional symptoms was higher in the DS+ASD group than the DS-only group in the present study (see Chapter 6, Table 6.2), the level reported in the DS+ASD group did *not* match that of the PLASN-R idiopathic ASD group (see Table 7.3). Therefore, although the presence of ASD appears to cause the children to experience emotional symptoms, the presence of DS perhaps mitigates the emotional symptom severity usually seen in idiopathic ASD. The fact that the levels of conduct problems and hyperactivity in the DS+ASD group matched those of the PLASN-R group is suggestive of the need for behavioural intervention with children with DS and co-morbid ASD, similar to those often implemented with young children with ASD (see Chapter 13, Section 13.4 for further discussion on interventions).

7.5 Limitations

Several limitations of the survey apply to the idiopathic ASD comparison. For example, only informant-based measures were used and recruitment of the children with DS through the Down's Syndrome Association may have resulted in sampling bias. In addition, the DS groups were not matched to the SCQ manual reference group. IQ measures were not utilised in the present study or by Berument et al. (1999) for the SCQ manual study, but the IQ of the DS group was likely to be lower. Furthermore, the SCQ manual reference group included some adults. Differences such as these may clearly have affected conclusions. However, the second idiopathic ASD group provided by the PLASN-R project were matched for age and verbal ability. Further, more general limitations of the study are discussed in Chapter 13, Section 13.2.

7.6 Conclusions

According to parent reports, children with DS and co-morbid ASD show a distinct autism profile compared with idiopathic ASD; many aspects of social interaction that are often impaired in people with ASD may be stronger in this group of children; however, they are more likely to display compulsions and rituals. The emotional symptoms and peer problems often experienced by people with ASD are reportedly less pronounced in children with DS and co-morbid ASD; however, high levels of conduct problems and hyperactivity are common to both groups.

PART C: GROUP STUDY

Chapter 8: Group study method

Outline

From the survey sample (Chapter 6), 50 children across the DS+ASD and DS-only groups were assessed using adaptive behaviour, autism profile and challenging behaviour outcome measures. Comparisons were made between the groups (DS+ASD vs. DS-only). This chapter outlines the method adopted for the comparative analysis, including key research questions, participants, response rates and outcome measures. Statistical analyses, details of ethical approval, and hypotheses are also reported.

8.1 Introduction

Although survey-based studies can be highly informative, in order to achieve a global understanding of behaviour a range of appropriate measures is required. The aim of this group study was to provide further insight into the behavioural phenotype of Down syndrome (DS) and co-morbid autism spectrum disorder (ASD) by employing detailed questionnaires, interviews and observational measures. The following research questions were considered:

1. What are the differences between the DS+ASD group and the DS-only group with respect to:
    a. adaptive behaviour skills
    b. autism profiles?

2. According to parent reports, what are the differences between the DS+ASD group and the DS-only group with respect to:
    a. challenging behaviour (including repetitive behaviour)
    b. functions of challenging behaviour?

3. What are the differences between the DS+ASD group and the DS-only group with respect to:
    a. educational placements
    b. challenging behaviour at school?

4. Are the following factors associated with the outcomes:
    a. age
    b. gender
    c. ASD severity
    d. adaptive behaviour level?

5. What factors affect whether a child attends a special needs school?

6. Are there differences in parent reports and teacher reports of challenging behaviour?

7. What is the range of individual differences within the DS+ASD group?

8.2 Participants

Inclusion criteria

Participants from the questionnaire survey (see Chapter 6) were ordered according to the child's total score on the Social Communication Questionnaire (SCQ) and split into quartiles. Participants from the top quartile (n=121) and the bottom quartile (n=121) were considered for the comparative analysis. Participants from the top quartile were referred to as the DS+ASD group and those from the bottom quartile as the DS-only group. Of the participants in the DS+ASD group 116 had consented to be contacted about further research; 109 participants from the DS-only group had given consent to be contacted.

Thirty three participants from the DS+ASD group initially agreed to take part (see Figure 8.1); however, 8 of these did not complete the research process. Therefore, data were collected for 25 participants for the DS+ASD group. The DS-only group (n=25) were matched to the DS+ASD group for age and gender, as far as possible. Recruitment was staggered in order to reduce the time period between the measures and to allow for monitoring of the gender ratio and mean age of the samples. Initially, preference was given to participants who resided in, or could be easily reached from, the South East of England due to ease of visits. However, the final sample came from locations all over England and Wales.

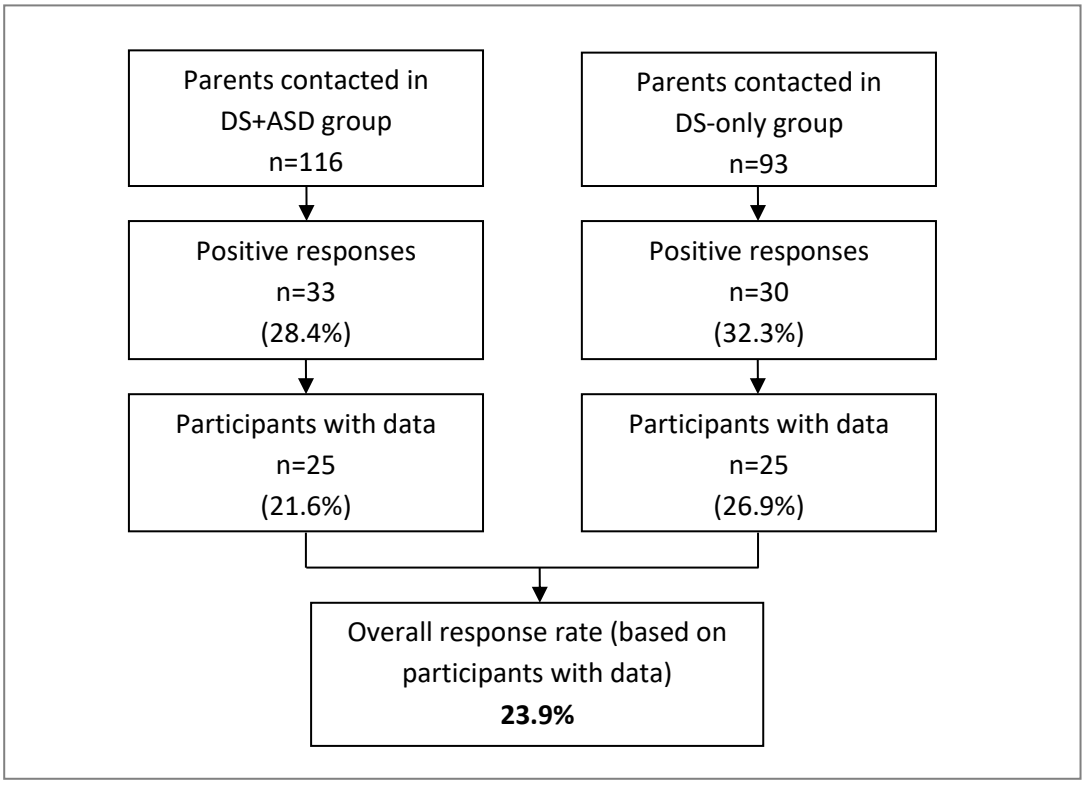

Figure 8.1 Response rates for the group study

Consent

A form indicating consent to be contacted about further research was included in the original questionnaire pack (see Chapter 6, Section 6.2.1). The preferred method of contact was stated on the form. Once approval was given by the participant to be involved in the group study, either by email or telephone, a second consent form (along with information sheets for parents and children) was sent out with further questionnaires. The second consent form had space for the child's school details. The completed form gave consent for the child to be involved in the group study and for the child's school to be contacted regarding a school visit (see Appendix C for copies of information sheets and consent form).

Further consent was sought from the head teacher of the school and the class teacher of the child; these forms were sent via post to the school with an information sheet and a cover letter inviting the school to take part in the study (see Appendix C for documents).

8.3 Structure of group study

The primary focus of the group study was to consider group differences (i.e. DS+ASD vs. DS-only). Differences were evaluated across adaptive behaviour, autism profiles, levels and functions of challenging behaviour (as indicated by parent reports), educational placements and challenging behaviour levels at school.

Subsequent consideration of factors independent of grouping which may impact on the findings (e.g. age, gender, adaptive behaviour level, ASD severity) was carried out. The factors that affect attendance at a special school, the extent of agreement between parent and teacher ratings of challenging behaviour and individual differences among the DS+ASD group were also explored.

8.4 Adaptive behaviour and autism measures

Vineland Adaptive Behaviour Scales, second edition (Vineland II; Sparrow, Cicchetti & Balla, 2005)

The Vineland II is a structured interview administered to parents and/or teaching staff to assess the child's skills across four domains: communication *(receptive, expressive, written),* daily living *(personal, domestic, community),* socialisation *(interpersonal relationships, play and leisure, coping)* and motor skills *(fine and gross)*. However, norms for motor skills are only available for children under 6 years (thus the motor skills scale was not used in the present study). There are 2 types of norm referenced scores available. There are standard scores for each domain, and v-scale scores for each subdomain. The v-scale scores have a mean of 15 and a standard deviation of 3 (possible range =1-24). A composite score of the sum of the 4 domain scores (3 domain scores when a motor skills score is not available) can be calculated in order to reflect overall functioning.

Internal consistency of the Vineland II is good for the age range of the present study (6-15 years) for domains (split-half analysis, r=.85-.95) and subdomains (r=.61-.93). Across the 3-6 years, 7-13 years and the 14-21 years age brackets, the test-retest mean correlations ranged from .75-.90 for domains and .67-.86 for subdomains (Sparrow et al., 2005). The psychometric properties of the original form (Sparrow, Balla & Cicchetti, 1984) have also been tested with a sample of children and adolescents with varying levels of intellectual disability (ID) (de Bildt et al., 2005a).

Although the Vineland II provides a reliable indication of a child's daily living skills, it is reliant on parent and/or teacher reports and therefore susceptible to bias.

Nevertheless, the Vineland II was considered appropriate for the present study as a measure of general ability (as opposed to IQ tests) since the intellectual functioning of children with DS and co-morbid ASD has been shown to be very low (Molloy et al., 2009) which would have resulted in severe floor effects on IQ measures and not allowed for comparison across the DS+ASD and DS-only groups. Furthermore, the Vineland II composite score has been proven to correlate strongly with IQ (Kanne et al., 2011).

Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000)

The ADOS-G is a semi-structured, standardised assessment of communication, social interaction, imagination, stereotyped behaviours and restricted interests for individuals suspected of having ASD. The ADOS comprises four modules; the appropriate module is selected based on the expressive language ability of the individual. A series of activities are carried out with the individual, which act as social presses to elicit certain behaviours. The behaviour of the individual is coded by the examiner. ADOS-G items are typically scored on a 3-point scale from 0 (*no evidence of abnormality related to autism*) to 2 (*definite evidence*). Some items include a code of 3 to indicate abnormalities so severe as to interfere with the observation. Each module has a diagnostic algorithm in which certain codings are selected and summed. Cut-off scores for autism and ASD are applied to the values produced for each individual. The ADOS-G has strong inter-rater and test-retest reliability (Lord et al., 2000), and a high level of agreement (77%) between ADOS-G diagnoses and clinical team diagnoses has been reported (Mazefsky & Oswald, 2006). (The ADOS, second edition [ADOS-2; Rutter et al., 2012] was not available when the present study began).

ADOS revised algorithms

Gotham et al. (2007) incorporated age into the diagnostic algorithms by dividing Module 2 into *'younger'* and *'older'* categories. The purpose of this was to address concerns regarding the sensitivity of the observation schedule relating to chronological age (de Bildt et al., 2004). Also, in order to make the ADOS groupings comparable to language level distinctions in the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter & Le Couteur, 1994), Gotham et al. (2007) divided module 1 into *'no words'* and *'some words'* categories. The communication and reciprocal social interaction scales were also combined to form a *'social affect'* scale, as there are reports from factor analyses that some non-verbal communication items and social items measure the same impairment (Constantino et al., 2004). Finally, restricted and repetitive behaviours were included in the total

algorithm score after the suggestion that they contribute to diagnostic stability (Lord et al., 2006). These changes relate to the recently published DSM-V (see Chapter 2, Section 2.2.1). Gotham et al. (2007) carried out exploratory factor analyses on each item in the protocol and formed new algorithms based around the reformed structure outlined above.

A follow-up study by Gotham et al. (2008) reported increased comparability between modules and improved predictive validity compared with the original algorithms. de Bildt et al. (2009) reported a more balanced sensitivity and specificity when using the revised algorithms; however, greater improvement in sensitivity and specificity was seen in modules 2 and 3 than in module 1. Kamp-Becker et al. (2013) also reported increased sensitivity when using the revised algorithm for module 3 with high-functioning children and adolescents with ASD. The revised algorithms *were* utilised in the present study.

ADOS Calibrated Severity Scores

In order to achieve ADOS scores that were less influenced by the demographics of the individual, and which could be compared across modules, Gotham, Pickles and Lord (2009) standardised the ADOS scores from a large sample (n=1,415) and created an autism severity metric. Gotham et al. (2009) took raw total percentiles corresponding to 3 ADOS classifications (Autism; PDD-NOS; Non-spectrum) and considered them against the age and language ability of the individuals to create calibrated severity scores (CSS). de Bildt et al. (2011) assessed the standardised scores in an independent Dutch sample and reported good discrimination between the classifications. The CSS showed good validity and proved more valuable than raw scores for comparability across groups. However, the CSS appeared more useful for module 1, and less so for module 3 (de Bildt et al., 2011). Shumway et al. (2012) also supported the use of the CSS; average severity scores remained stable across modules for children within each diagnostic group. These findings support inter-module comparisons with cross-sectional data. The CSS *were* utilised in the present study.

8.5 Behavioural measures

Developmental Behaviour Checklist –Primary Carer Report (DBC-P; Einfeld & Tonge, 2002)

The DBC-P assesses a wide range of behavioural and emotional disturbances in children with ID aged 4-18 years. It has 96 items rated by parents/carers on a 3-point scale (0=*not true as far as you know*, 1=*somewhat or sometimes true*, 2=*very true or often true*). The

items were derived from clinical records of behavioural concerns and can be categorised into the following 5 subscales: *disruptive / antisocial, self-absorbed, communication disturbance, anxiety*, and *social relating*. The DBC-P has shown good reliability; an inter-rater study, in which each parent of a child completed the form, produced a correlation of .80. Internal consistency of the DBC-P is also good (split-half analysis, r=.90). Factor analysis of the DBC-P resulted in the items loading onto the 5 aforementioned subscales, which accounted for 43.7% of the total variance (Einfeld & Tonge, 2002).

Challenging Behaviour Questionnaire (CBQ; Hyman, Oliver & Hall, 2002)

The CBQ is a brief questionnaire that evaluates the presence or absence of different forms of challenging behaviour. The form covers *self-injury, physical aggression, destruction of property* and *stereotyped behaviours*. Examination of the psychometric properties of the questionnaire has shown good inter-rater reliability with reliability coefficients ranging from .61 to .89 (Hyman et al., 2002). After consideration of the literature on the behavioural phenotype of children with DS, an additional behaviour of *refusal to comply* was added to the form for the purpose of the present study. Many children with DS are depicted as "stubborn" (Dykens, 2007) which can be a particular challenge to parents, and thus this item was incorporated into the measure of challenging behaviour.

Repetitive Behaviour Questionnaire (RBQ; Moss et al., 2009)

The RBQ is a 19 item informant questionnaire used to measure the frequency of repetitive behaviours over the preceding month. There are 5 subscales: *stereotyped behaviour, compulsive behaviour, insistence on sameness, restricted preferences,* and *repetitive speech* each rated on a 5-point scale ranging from *'never'* to *'more than once a day'*. Those behaviours which occur *'once a day'* or *'more than once a day'* are deemed to be of clinical importance; thus, item-level cut-off is attained if an individual scores ≥3 on an item. Each repetitive behaviour is defined in terms of discrete observable behaviours, does not describe involuntary movements such as tics and does not describe sensory behaviours such as sniffing, licking or touching. Certain items on the RBQ require the individual to be verbal. For the present study, verbal ability was determined by the *'able to talk using short phrases or sentences'* item on the SCQ. Non-verbal children were excluded from analyses on the *restricted conversation, repetitive questions* and *echolalia* items, the corresponding subscales (i.e. *restricted preferences* and *repetitive speech*) and the *total repetitive behaviour* scale. Inter-rater reliability of the RBQ is good (r=.46-.80) (Moss et al., 2009), with 73% of items above .60. Test-retest reliability is also good (r=.61-.93), with 53% of

items above .80. Internal consistency for some of the subscales is relatively low (e.g. *restricted preferences* (α=.50) and *repetitive speech* (α=.54)) which has been attributed to behaviours grouping together in terms of function as well as form (Moss et al., 2009). Nevertheless, internal consistency is good at the full-scale level (α >.80).

Questions about Behavioral Function –Modified (*QABF-M; Oliver & Richards, 2009)*

The QABF-M is a 40 item questionnaire used to explore associations between challenging behaviour and environmental events that have been associated with behavioural difficulties in individuals with intellectual disability. The QABF-M is an extended version of the original form (Matson & Vollmer, 1995). In addition to the original functions of: (1) *self-stimulation*; (2) *demand escape*; (3) *access to tangibles*; (4) *attention*; and (5) *relief of pain or discomfort*, the extended form also considers: (6) *sensory*; (7) *routine*; and (8) *social escape*. These latter functions have been associated with behavioural difficulties in individuals with ASD, and thus the extended form was considered appropriate for use in the present study. Parents were asked to complete the questionnaire form with the behaviour they find most challenging in mind. Scores for each of the 8 functions of behaviour were used to determine the principal functions for each child.

8.6 Teacher reports and natural observation

Developmental Behaviour Checklist –Teacher Report (*DBC-T; Einfeld & Tonge, 2002)*

The DBC-T is a 94 item checklist that shares the same response format as the DBC-P but is administered to teachers and/or teaching assistants. All items have a counterpart on the DBC-P, except for 3 items about sleep disturbance that have been removed and 1 item that has been added, “Unpopular with other children.”

Factor analysis of the DBC-T produced a similar output to that of the DBC-P; therefore, in order to facilitate direct comparison between the measures, the DBC-P factor solution was applied to the DBC-T. The DBC-T has a lower level of inter-rater reliability than the DBC-P (teacher vs. teaching assistant, r=.60) (Einfeld & Tonge, 2002). The variation in these accounts may be due to the proximity and intensity of the relationship between the member of staff and the child. Often, a teaching assistant will work more directly with an individual child than the class teacher and may therefore have greater insight into the behaviours of the child. In order to achieve the most reliable account for

the present study we asked for a member of staff who knew the child well to complete the form. There is also poor agreement between teacher and parent reports (r=.30) (Einfeld & Tonge, 2002). However, this difference has been observed on many other measures of childhood problems and has been attributed to actual differences in behaviour as well as the frame of reference of the reporter (Mitchell & Shepherd, 1966).

Natural observation method

The children were observed in their school environment for a duration of 1.5 hours[25]. Breaks in observation (e.g. due to toilet breaks) meant that the observation was often not continuous in nature. The observation was carried out as unobtrusively as possible, with as little interaction between observer and child as possible. Staff members were asked to interact with the child as normal and activities typical of the school setting (e.g. group activities, individual activities, play time and meal times) were observed. Situational settings and challenging behaviours were recorded on a Lenovo E530 Thinkpad using the Obswin program[26] (Martin, Oliver & Hall, 2000). For the purpose of inter-rater reliability several of the cases were videotaped. Video recording was carried out on a Sony DCR-SX33 Handycam with a LCD fold out screen, which was utilised to minimise observer reactivity (Sloneem et al., 2009).

Natural observation definitions

Three situational settings were recorded: *group* (participant is within 1 metre of 1 or more peers, in a structured activity), *1-to-1* (participant is accompanied by 1 staff member only who is guiding them through an educational or structured activity), *play* (no structured activity is enforced; materials may be available). If the child was involved in a structured activity with peers, even though accompanied by an adult who was employed as 1-to-1 support, this was coded as a 'group' activity. Lunchtime sessions were split across 'group' and 'play' because some lunchtime sessions (often in special need environments) were highly structured in nature and the children were given a lot of direction (as in the classroom), whereas others (although supervised) allowed the child to act freely. The challenging behaviours that were recorded are displayed in Table 8.1.

[25] Four children were excluded from this analysis as they were visited at home at the request of the caregiver. A further 4 were excluded as the school and/or caregiver did not consent to taking part in this part of the research study.

[26] Obswin (Martin et al., 2000) is a computer program designed for the collection and analysis of observational data. By using onsets and offsets, the program allows continuous recording of the frequency and duration of environmental events and behavioural responses. Situational settings can also be applied to the data. The program can be used in real time or linked to a video file.

Situational settings were based on previous observations of this kind (e.g. Moss et al., 2005). The forms of challenging behaviour were based on the CBQ (see Section 8.5, p.117). Behaviours were kept relatively broad[27] in order to reduce data (to aid reliable recording), while still allowing topographically related comparisons to be made. Behaviours were not mutually exclusive; for instance, a child could be shouting in the face of another whilst flapping their hands which would be coded as 'aggression' and 'stereotyped behaviour'.

Table 8.1 Challenging behaviours recorded during the natural observation

Challenging behaviour	Description	Examples
Aggression	Verbal statements or non-accidental physical acts which are likely to induce fear or stress	Shouting/loud vocalisation in the face of another, hitting another
Destruction of property	A non-accidental physical act which results in superficial or substantial damage to any property or the environment	Throwing classroom items e.g. books, kicking structures e.g. fence in playground
Refusal to comply	The active* evasion of a task or instruction *that excludes all other forms of challenging behaviour*	Answering "no" when asked to do something, pulling an item away when asked to hand it over
Self-injurious behaviour	Non-accidental behaviours which result in injury to the child	Hitting self, scratching self, banging head
Stereotyped behaviours	Apparently meaningless, repetitive movements which are executed in an almost identical way each time	Hand flapping, twiddling item in hand, repetitive tapping of item

*Care must be taken to only include examples where the child has clearly understood the request.

8.7 Statistical analysis

The Statistical Package for the Social Sciences (SPSS) Version 20.0 was used for data analysis. Data were entered into the database (accessed only by a password) using identification numbers to retain participant anonymity. Hard copies of the data were stored in a locked filing cabinet at the Institute of Psychiatry.

For the natural observation, percentage occurrences of each form of challenging behaviour were calculated in Obswin for each child. The data were transferred to SPSS version 20.0 and collated according to the DS-only (n=26; 39 hours) and DS+ASD (n=16;

[27] Opposed to specific behaviours such as self-biting, self-striking, scratching (which would all appear under 'self-injurious behaviour' in the present study

24 hours) grouping. All data were tested for normality using Kolmogorov-Smirnov tests and visual inspection of histograms. Homogeneity of variance between the comparison groups (i.e. DS+ASD and DS-only) was tested using Levene's tests. If the data were normal and homogeneity of variance achieved parametric tests (e.g. t-tests) were utilised. However, if these assumptions were violated non-parametric tests (e.g. Mann Whitney U tests) were utilised. In the latter case, if homogeneity of variance was not achieved this was noted and findings interpreted cautiously as, although by virtue of ranking the data Mann Whitney U tests reduce the impact of outliers, there is still some suggestion that the underlying distributions should be similar in shape (Sheskin, 2003). When Mann Whitney U tests were used the standardised z statistic was reported. Chi-square tests were used to assess the association between categorical variables, with Fisher's exact statistic reported when ≥20% of the cells had an expected count less than 5.

Correlation analysis was used to assess associations between the outcomes and factors such as child age (Pearson's r for normal data, Spearman's rho for skewed data). In circumstances where a covariant had been identified in a prior analysis and needed to be controlled for, partial correlation analysis was adopted. Regression analysis was used to assess the contribution of the adaptive behaviour level of the child (i.e. Vineland II composite) on the outcome of the ADOS-G (i.e. domain and total scores). Regression was the preferred method of statistical analysis because, unlike partial correlations, it describes the direction of the relationship. Prior to conducting the regression analysis it was established that the independent variable (i.e. Vineland II composite) was significantly correlated with the outcome variables (i.e. r≥ .30) to ensure that the independent variable was likely to have predictive value. Molloy et al. (2009) utilised a similar method to assess the impact of intelligence on the outcome of the ADI-R in children with Trisomy 21 with and without autism. Molloy et al. (2009) conducted an analysis of covariance (ANCOVA) to adjust for intelligence scores to determine whether a group difference remained. This statistical method was *not* adopted in the present study because the assumption that the relationship between the ADOS-G scores and the Vineland II composite did not vary by group was violated.

Path analysis was adopted to assess the factors affecting whether or not a child attended a special school. Based on a paper by de Bildt et al. (2005b), which explored the level of education in children and adolescents with intellectual disability (ID), the factors evaluated were: adaptive behaviour (i.e. Vineland II composite score), behaviour problems (i.e. DBC-T total behaviour problems) and ASD severity (i.e. ADOS calibrated severity score (CSS)). The teacher report on the DBC was chosen over the primary carer report

given the focus on the school setting. First, group differences (mainstream vs. special) were assessed for the proposed factors. Then regression analysis was carried out to assess which factors directly influenced whether or not the child attended a special school. Stepwise logistic regression was adopted and all of the variables listed above were entered at the same time. Based on the outcome of the regression analysis, a path analysis was constructed in AMOS (version 21). The path was constructed based on the model proposed by de Bildt et al. (2005b) using the equivalent measures outlined above (this was the only model tested). The purpose of the group comparisons was to ensure that only independent variables that were likely to have predictive value were included in the regression analysis. The purpose of the regression analysis was to assess the applicability of the de Bildt et al. (2005b) model to the present study.

Agreement between parent reports and teacher reports on the DBC was assessed using intra-class correlations. The intra-class correlations were based on absolute agreement, and average measures were used. The 2-way-random model was applied as both the children and the raters (i.e. teachers) varied. They were interpreted according to criteria set by Shrout and Fleiss (1979) by which scores above .75 are acceptable.

Evaluation of individual differences within the DS+ASD group was conducted by visual inspection of box plots and the comparison of Mean or Median Absolute Deviation (MAD) scores. Absolute deviation was calculated around the mean for normal data, and around the median for skewed data. The MAD was selected because it is an efficient way to assess variability within a data set.

Significance level

As numerous tests were performed in the group study, to reduce the chance of obtaining type I errors (i.e. false positive results), statistical significance was determined by a p-value of <.01 and p-values of <.05 were noted as "marginally significant" or a "marginal difference". This correction method was based on statistical advice and chosen over the Bonferroni correction because the latter has been subject to criticism for being too conservative and resulting in type II errors (i.e. false negative results) (Nakagawa, 2004). Effect sizes (Cohen's r for t-tests, Cliff's d for Mann-Whitney U tests, and Cramer's V/Phi (φ) for Chi-square tests) are also reported. Effect sizes were interpreted according to Cohen's benchmarks of small=.10, medium=.30, and large=.50 (Field, 2005). Equations used to calculate effect sizes can be found in Appendix B (see Chapter 6, Section 6.2.5, p.68 for justification of the choice of effect sizes).

Power analyses

The goal of the proposed study was to test the null hypothesis that the 2 population means were equal. The criterion for significance (alpha) was set at .05. The tests were 2-tailed, so an effect in either direction could be interpreted. Results from previous research into DS and co-morbid ASD were utilised so that reasonable effect sizes, which could be anticipated in the current study, were used in the power analyses. The first power analysis was based on a DS+ASD/DS-only group difference observed on the Stereotyped Behaviour subscale of the RBQ by Moss et al. (2013b). The computation assumed the mean difference was 5.44 (corresponding to means of 7.00 and 1.56), the effect size was 1.41, and the common standard deviation was 3.86. With power of 95%, the proposed sample size was 15. The second power analysis was based on a DS+ASD/DS-only group difference observed on the Social Interaction subscale of the Autism Diagnostic Interview-Revised by Magyar et al. (2012). The computation assumed the mean difference was 6.58 (corresponding to means of 18.61 and 12.03), the effect size was 1.04, and the common standard deviation was 6.30. With power of 95%, the proposed sample size was 25. A sample size of approximately 25 per group was deemed to provide sufficient power to find group differences in the present study.

Missing data

For the DBC-P, DBC-T and QABF-M missing items were prorated at subscale level if the informant completed 75% of the relevant subscale. As directed by the authors, missing items on the RBQ were prorated at subscale level if the informant completed 65% of the relevant subscale (Moss et al., 2009). For the CBQ missing items were not assessed for that participant. As directed by the manual, if during the ADOS-G the child had no opportunity to display the characteristic being coded then a score of 9 was given, which equated to 0 in the algorithm. If the coding was not applicable to the child (e.g. the frequency of their speech was inadequate, or they had limitations due to a physical disability) then a score of 8 was given, which also equates to 0 in the algorithm.

Reliability

Inter-rater reliability for ADOS-G scores was completed for 24.0% of the sample (n=12). The subsample was representative of the overall sample as the subsample and overall sample were matched for age ($t(60)=.30$, $p=.77$, $r=.04$) and gender (Fisher's exact, $p=.57$). The children in the subsample were selected across both the DS-only and DS+ASD groups.

(Subsample characteristics can be found in Appendix C). The intra-class correlation[28] for the ADOS-G total score (according to the revised algorithms) was .90 (95% CI=.40-.98). The mean intra-class correlation at algorithm domain level was .81 (*social affect*=.90, *restricted and repetitive behaviours*=.71). At item level, once items were converted into the algorithm values (i.e. 0=0, 1=1, 2=2, 3=2 and 7/8/9 =0) weighted kappa=.61 (95% CI=.53-.69). The second rater (ES) tended to award more codes with an algorithm value of 2 (see Appendix C for a stacked histogram); a post-hoc marginal homogeneity test ($p<.001$) confirmed this bias.

Inter-observer reliability was also calculated for the natural observation of challenging behaviours. Inter-observer agreement was calculated for 26.2% of the observations (n=11; 16.5 hours). Kappa values were calculated for the presence of each behavioural code on a 10-second interval-by-interval basis by Obswin (a recognised method in observational research, see Oliver et al. (2009) as an example). The subsample was representative of the overall sample as the subsample and overall sample were matched for age ($t(51)=-1.05$, $p=.30$, $r=.15$) and gender (Fisher's exact, $p=.39$). The children in the subsample were selected across both the DS-only and DS+ASD groups and included a live coded example. (Subsample characteristics can be found in Appendix C). The mean Kappa score was .79 (*aggression*=.90, *destruction of property*=.78, *refusal to comply*=.93, *self-injurious behaviour*=.67, *stereotyped behaviours*=.67). Complete agreement was achieved on the situational setting of the observations.

8.8 Ethical approval

Ethical approval for the study was granted to Georgina Warner by the Psychiatry, Nursing & Midwifery (PNM) Research Ethics Subcommittee in February 2012 (Project Reference: PNM/11/12-45). Ethical approval for subsequent modifications to the project was also granted by the PNM Research Ethics Subcommittee in July 2012. (See Appendix C).

[28] Intra-class correlations were based on absolute agreement, and average measures were used. The 2-way-mixed model was applied as the children varied but the raters (i.e. GW and ES) remained fixed.

8.9 Hypotheses

Based on previous research findings, several hypotheses were made about: (1) the group comparisons, (2) associated factors aside from clinical grouping.

1. Compared with children with DS only, children in the DS+ASD group:
   a) will display greater overall impairment in adaptive behaviour as measured by the Vineland II
   b) will show greater impairment across the autism domains (i.e. social affect and restricted and repetitive behaviour) on the ADOS-G
   c) will be reported to show higher levels of challenging behaviour and repetitive behaviours by parents on the DBC-P, CBQ and RBQ
   d) will be more likely to engage in challenging behaviour for the purpose of *self-stimulation,* for *sensory* reasons, because there has been a *break in routine* or for *social escape* (as measured by the QABF)
   e) will be more likely to attend a special needs (opposed to mainstream) school
   f) will be reported to show higher levels of challenging behaviour at school on the DBC-T

2. Across both groups:
   a) younger children will be more likely to be self-absorbed and anxious as measured by the DBC (based on the DBC manual)
   b) boys will be more likely to display social relating problems as measured by the DBC (based on the DBC manual)
   c) children with greater ASD severity will be more likely to have poorer adaptive behaviour skills (as measured by the Vineland II) and to display challenging behaviours (as measured by the DBC)
   d) the level of adaptive behaviour skills (as measured by the Vineland II) will affect outcomes on the ADOS-G

Chapter 9: Group study results

Outline:

The classification of comparison groups (DS+ASD and DS-only) is outlined and group characteristics described. The results are presented in the following order:

1. Group comparisons:
    a.) Adaptive behaviour skills and autism profiles
    b.) Challenging behaviour from the parent perspective
    c.) Educational placements and challenging behaviour at school
2. Associated factors aside from clinical grouping
3. Factors that affect attendance at a special school
4. Differences in parent and teacher reports of challenging behaviour
5. Individual differences among children in the DS+ASD group

9.1 Group classification and characteristics

Initial classification of participants (DS+ASD vs. DS-only) was based on individuals' total score on the Social Communication Questionnaire (SCQ) (see Chapter 8, Section 8.2, p.112). The groups were matched for age and gender. Although the DS+ASD group were marginally older and had slightly more males, the p values indicated that the differences were not significant and the effect sizes were small. The DS+ASD group, as expected, scored significantly higher on the SCQ than the DS-only group (see Table 9.1).

Table 9.1 Age, gender and SCQ total scores for the DS+ASD and DS-only recruited groups

		DS+ASD	DS-only	Group difference
N		25	25	
Age in years	Mean (SD) Range	12.16 (2.98) 8-17	11.36 (2.62) 8-17	t (48)=-1.01, p=.32, r=.14
Gender	% Male (N)	68.00 (17)	60.00 (15)	χ^2(1, N=50) =.35, p=.56, φ=.08
SCQ score	Mean (SD) Range	24.81 (4.28) 18-32	4.14 (1.88) 1-7	t (32.98)=-22.07, **p<.001**, r=.97

However, following their assessments on the Autism Diagnostic Observation Schedule-Generic (ADOS-G) to confirm the presence of ASD, a number of participants appeared to have been misclassified by the SCQ (i.e. 8 with positive scores on the SCQ scored below threshold on the ADOS-G; 6 with negative scores on the SCQ scored above the ADOS-G threshold (see Chapter 10 for further exploration of these issues). Since the ADOS-G is much more detailed, objective and considered to a more accurate measure of the presence of ASD than screening instruments such as the SCQ (DiGuiseppi et al., 2010; Schanding et al., 2012) grouping was reassigned according to the ADOS-G output (see Table 9.2).

When the groups were restructured in this way (Table 9.2) the DS+ASD group had a slightly higher mean age, as well as proportion of males; however, the differences were not significant according to p values. The mean SCQ score of the DS+ASD group remained significantly higher.

Table 9.2 Age, gender and SCQ total scores for the DS+ASD and DS-only restructured groups *(All DS+ASD children above threshold on ADOS-G; all DS-only children below threshold)*

		DS+ASD	**DS-only**	**Group difference**
N		23	27	
Age in years	Mean (SD) Range	12.39 (2.82) 8-17	11.22 (2.74) 8-17	t (48)=-1.48, p=.14, r= .21
Gender	% Male (N)	73.90 (17)	55.60 (15)	χ^2(1, N=50)=1.82, p=.18,φ=.19
SCQ score	Mean (SD) Range	20.68 (10.43) 2-32	9.19 (8.41) 1-27	t (48)=-4.31, **p<.001**, r=.53

Finally, because of the discrepancy in 14 cases between SCQ and ADOS-G ratings, a further reclassification included only those children meeting/not meeting threshold on *both* measures. This resulted in 17 children in the DS+ASD group and 19 in the DS-only group. Within this 'consistent' group the DS+ASD children still had a slightly higher mean age and higher proportion of males; however, the differences remained non-significant. The mean SCQ score of the DS+ASD group was significantly higher, as before (see Table 9.3).

Table 9.3 Age, gender and SCQ total scores for the DS+ASD and DS-only consistent groups *(All cases with discrepancy between measures excluded)*

		DS+ASD	DS-only	Group difference
N		17	19	
Age in years	Mean (SD) Range	12.65 (3.08) 8-17	11.26 (2.84) 8-17	t (34) =-1.40, p=.17, r=.23
Gender	% Male (N)	70.60 (12)	52.60 (10)	χ^2(1, N=36)=1.22, p=.27,φ=.18
SCQ score	Mean (SD) Range	26.37 (4.06) 19-32	4.01 (1.97) 1-7	t (22.58) =-20.64, **p<.001**,r=.97

The findings reported in this thesis are based on the restructured groups of children according to their ADOS-G scores (n=23 above and n=27 below threshold; Table 9.2). However, all central analyses were run a second time using only those participants whose ADOS-G and SCQ scores were consistent (i.e. children in Table 9.3, the "consistent" groups) and differences were presented in footnotes.

9.2 Group comparisons

Section 9.2.1 Adaptive behaviour and autism profiles

Research question 1: What are the differences between the DS+ASD group and the DS-only group with respect to:

a.) adaptive behaviour skills

b.) autism profile?

Adaptive behaviour

Supporting Hypothesis 1.a., children in the DS+ASD group scored lower, on average, than the DS-only group on the Vineland II composite score (t(45)=5.34, **p<.001**, r=.62) and on all three subscales (*communication*: t(45)=5.60, **p<.001**, r=.64; *daily living*: t(45)=4.98, **p<.001**, r=.60; *socialisation*: t(45)=4.72, **p<.001**, r=.58) (see Figure 9.1), indicating greater overall impairment in the DS+ASD group[29].

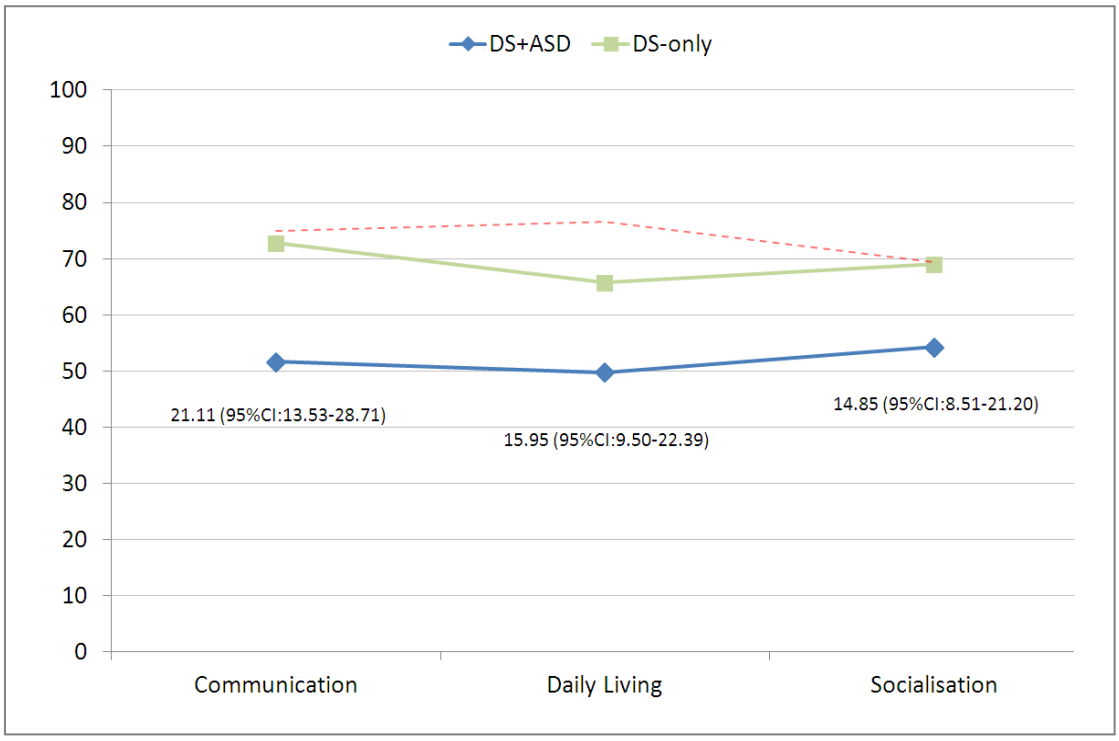

Figure 9.1 Adaptive behaviour profiles of DS+ASD and DS-only groups, mapped by mean Vineland II subscale scores. Mean differences and 95% confidence interval (CI) of differences are reported. (Red dashed line indicates profile of children with idiopathic ASD aged 9-17, based on mean Vineland II subscale scores; Kanne et al., 2011).

[29] Group differences remained when the "consistent" groups (i.e. SCQ+ADOS ratings in agreement) were compared.

Autism profiles

Supporting Hypothesis 1.b., children in the DS+ASD group scored higher, on average, than the DS-only group at total and domain level on the ADOS-G (see Figure 9.2)[30].

At item level (see Figure 9.3), the DS+ASD group were significantly more impaired on the following items: *overall level of language* (z=3.83, **p<.001**, Cliff's d=.67), *gestures* (z=3.77, **p<.001**, Cliff's d=.59), *eye contact* (z=2.81, **p<.01**, Cliff's d=.35), *facial expressions* (z=4.43, **p<.001**, Cliff's d=.62), *shared enjoyment* (z=4.10, **p<.001**, Cliff's d=.52), *quality of social overtures* (z=4.61, **p<.001**, Cliff's d=.72), *imagination/creativity* (z=4.85, **p<.001**, Cliff's d=.77), *sensory interests* (z=3.92, **p<.001**, Cliff's d=.59), *hand stereotypies* (z=3.71, **p<.001**, Cliff's d=.56), *excessive interests* (z=2.79, **p<.01**, Cliff's d=.39) and *aggression* (z=3.47, **p<.005**, Cliff's d=.44). Marginal significance[31] was achieved for group differences on the *intonation* (z=2.45, **p<.05**, Cliff's d=.46) and *overactivity* (z=2.20, **p<.05**, Cliff's d=.33) items.

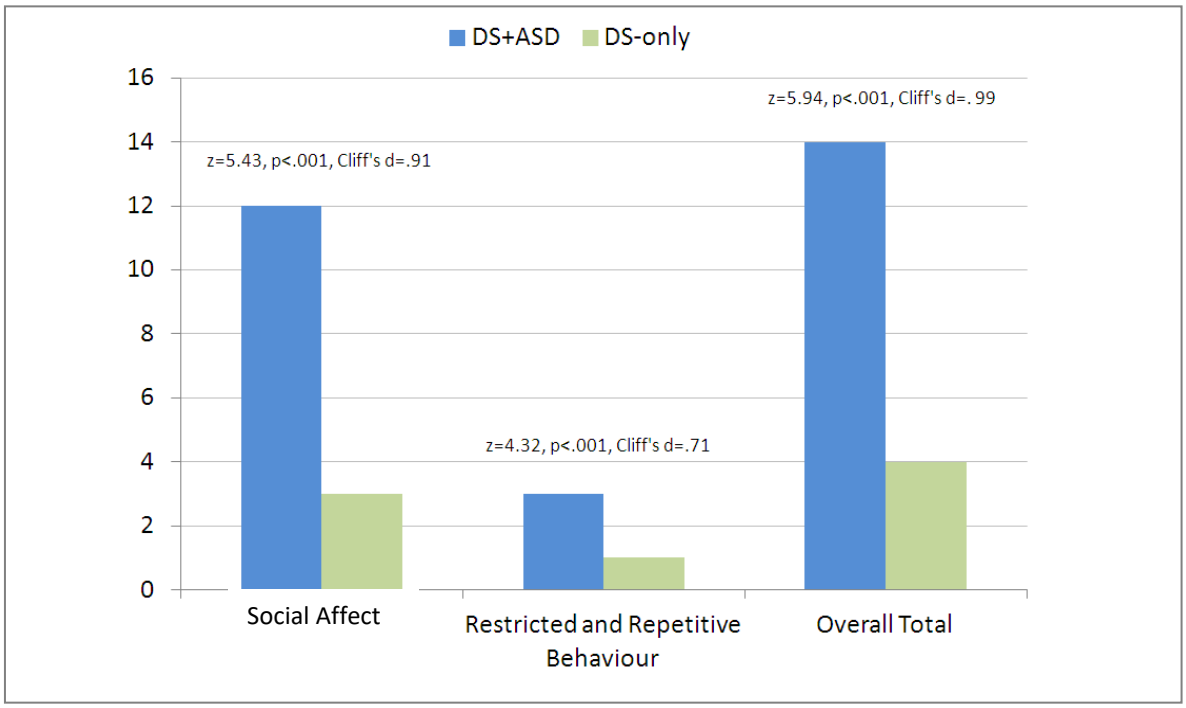

Figure 9.2 Median ADOS-G domain scores (revised algorithms)

[30] Group differences remained when the "consistent" groups were compared.
[31] See Chapter 8, Section 8.7, p.122 for an explanation on how significance was determined.

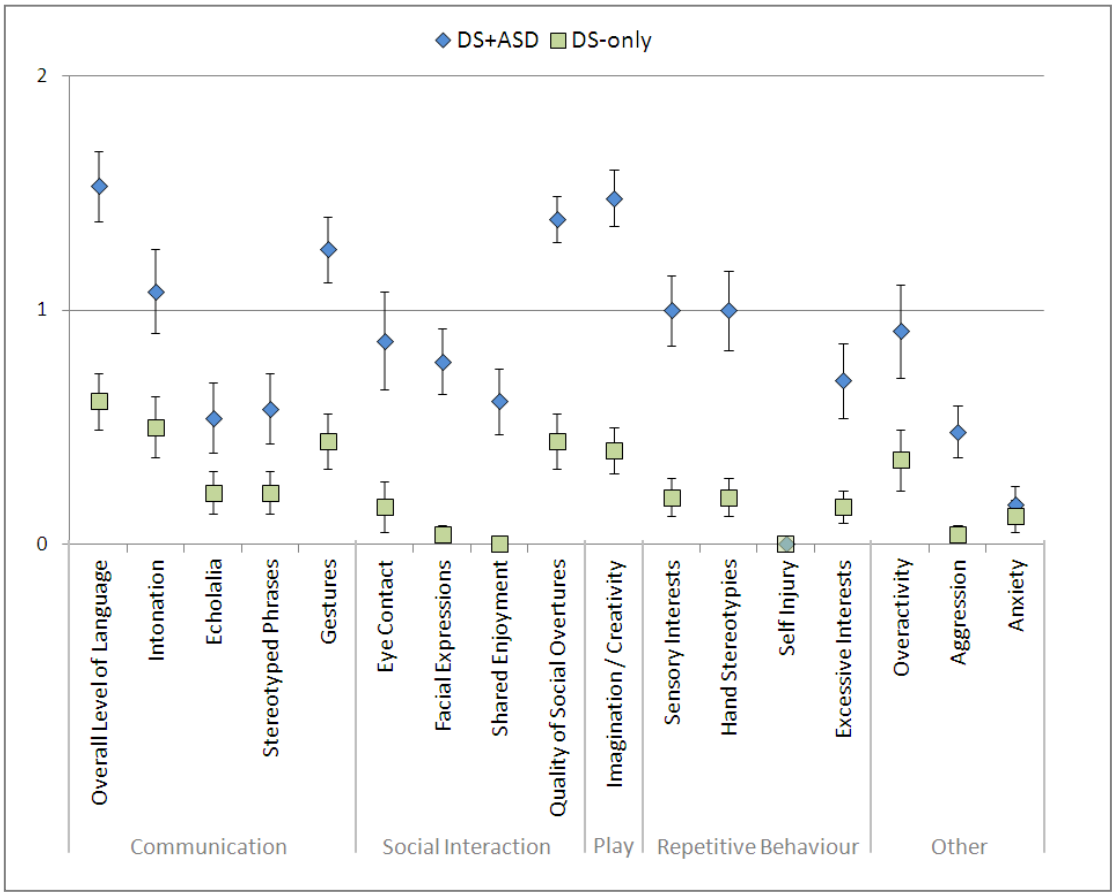

Figure 9.3 Mean ADOS-G item level scores. A higher score = greater severity of impairment. Only items which are shared across modules 1 to 3 are included. Mean scores reported due to uninformative nature of median scores. Error bars indicate the standard error of the mean.

Section 9.2.2 Challenging behaviour from the parent perspective

Research question 2: According to parent reports, what are the differences between the DS+ASD group and the DS-only group with respect to:

a.) challenging behaviour (including repetitive behaviour)

b.) functions of challenging behaviour?

Challenging behaviour

As predicted by Hypothesis 1.c. (and illustrated in the following sections), children in the DS+ASD group tended to have higher scores on parent measures of problem behaviours.

Developmental Behaviour Checklist-Primary Carer Report (DBC-P)

Children in the DS+ASD group scored higher, on average, than the DS-only group for *total behaviour problems* (z=2.92, **p<.005**, Cliff's d=.48). They also had higher scores on the *self-absorbed* subscale (Figure 9.4). Marginally significant group differences were seen on the *communication disturbance* and *social relating* subdomains[32].

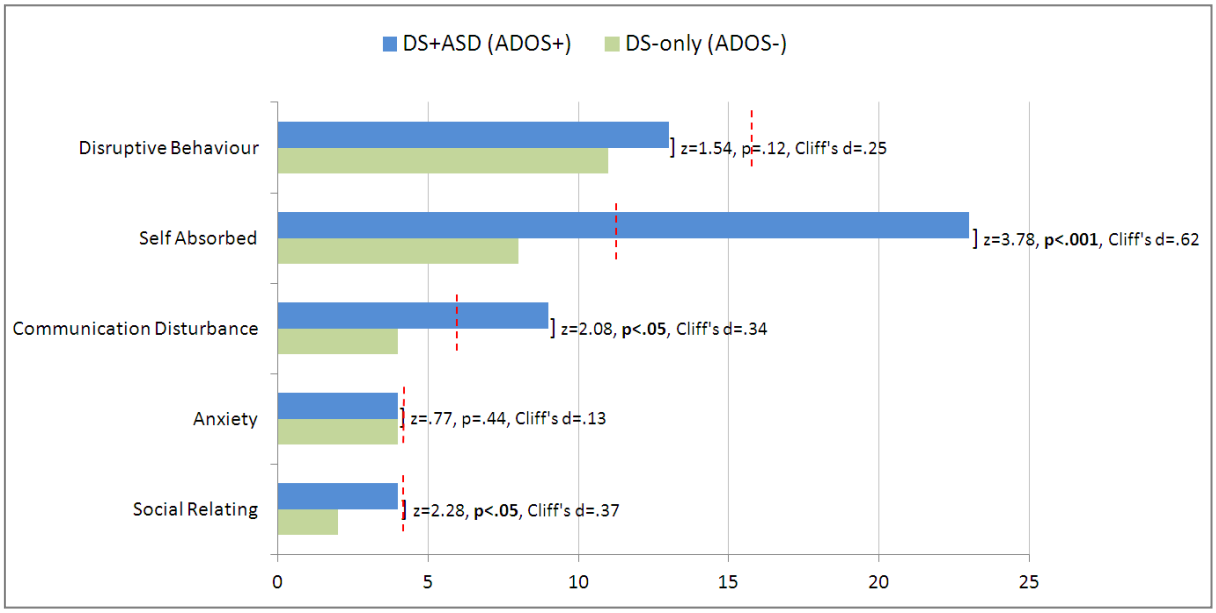

Figure 9.4 Median scores for the DS+ASD and DS-only groups on the DBC-P subscales

(Red dashed lines indicate mean scores for individuals with a mild intellectual disability (IQ 50-70), as outlined in the DBC manual; Einfeld & Tonge, 2002)

[32] Comparison of the "consistent" groups resulted in differences on *all* scales, including marginally significant differences on the *disruptive* subscale (z=2.03, **p<.05**, Cliff's d=.27) and the *anxiety* subscale (z=2.27, **p<.05**, Cliff's d=.25).

Challenging Behaviour Questionnaire (CBQ)

On the CBQ, s*elf-injury* and *physical aggression* were reported more commonly in the DS+ASD group than the DS-only group (see Table 9.4). Marginally significant group differences were also seen in the levels of *destruction of property* and *stereotyped behaviour*.

In the subsamples of children who were reported to display the challenging behaviours, the need for 'physical contact, prevention or restraint' only differed between the groups for *refusal to comply* (z=3.39, **p<.005**, Cliff's d=.57). Median scores indicated that physical contact, prevention or restraint (due to their refusal to comply) was necessary for the DS+ASD group *weekly* (i.e. score of 3), whereas for the DS-only group it was *never* necessary (i.e. score of 1) (see Appendix C for CBQ median scores relating to the need for physical contact, the frequency of behaviours and the longest episode).

The frequency of the behaviours only differed (at a marginal level) for *refusal to comply* (z=2.33, **p<.05**, Cliff's d=.40). Median values indicated that the DS+ASD group would display the behaviour *daily* (i.e. score of 3), whereas the DS-only group would display the behaviour *weekly* (i.e. score of 2). The longest episode only differed (at a marginal level) between the groups (DS+ASD vs. DS-only) for *destruction of property* (z=2.37, **p<.05**, Cliff's d=.33). Median scores indicated that the destruction of property by children in the DS+ASD group tended to last *less than 5 minutes* (i.e. score of 2), whereas the destruction of property by children in the DS-only group would last *less than 1 minute* (i.e. score of 1).

Table 9.4 Percentage occurrence of challenging behaviours in the DS+ASD and DS-only groups, according to the CBQ

Challenging behaviour	**Group**	**% (n)**	**Group difference**
Self-injury	DS+ASD	43.48 (10)	
	DS-only	00.00 (0)	$\chi^2(1, N=50) = 14.67$, **p<.001**, $\varphi = .54$
Physical aggression	DS+ASD	60.87 (14)	
	DS-only	14.81 (4)	$\chi^2(1, N=50) = 11.43$, **p<.005**, $\varphi = .48$
Destruction of property	DS+ASD	52.17 (12)	
	DS-only	14.81 (4)	$\chi^2(1, N=50) = 7.97$, **p<.05**, $\varphi = .40$
Stereotyped behaviour	DS+ASD	63.64 (14)	
	DS-only	29.63 (8)	$\chi^2(1, N=49) = 5.67$, **p<.05**, $\varphi = .34$
Refusal to comply	DS+ASD	95.65 (22)	
	DS-only	81.48 (22)	$\chi^2(1, N=50) = 2.36$, $p = .12$, $\varphi = .22$

Repetitive Behaviour Questionnaire (RBQ)

(Note that children who were unable to *'talk using short phrases or sentences'* (according to the SCQ) (n=12) were excluded from analyses on the *restricted conversation*, *repetitive questions* and *echolalia* items, the corresponding subscales (i.e. *restricted preferences* and *repetitive speech*) and the *total repetitive behaviour* scale).

Compared with the DS-only group, children in the DS+ASD group were reported to show marginally higher levels of *total repetitive behaviour* (t(34)=-2.75, **p<.05**, r=.43)[33]. At subscale level, the DS+ASD group were reported to show higher levels of *stereotyped behaviour* and marginally higher levels of *repetitive speech* than the DS-only group (Table 9.5)[34].

At item level, the DS+ASD group were reported to show higher levels of *object stereotypy* (z=2.77, **p<.01**, Cliff's d=.41), *body stereotypy* (z=3.21, **p<.005**, Cliff's d=.46) and *hand stereotypy* (z=2.88, **p<.005**, Cliff's d=.42). Marginal group differences were also seen in *preference for routine* (z=2.32, **p<.05**, Cliff's d=.36) and *repetitive phrases/signing* (z=2.56, **p<.05**, Cliff's d=.34). Figure 9.5 demonstrates the profile of item level scores for each of the groups. The mean item scores are presented on radar charts (for the DS+ASD group and DS-only group respectively). The items have been colour blocked to represent the subscales of the RBQ. (See Moss et al., 2009 for a similar presentation of RBQ profiles across various genetic disorders).

Further item level analysis was conducted using clinical cut-off scores (i.e. on the proportions of children meeting item level clinical cut-off of ≥3). The clinical cut-off analysis supported the item level analysis (i.e. *object stereotypy, body stereotypy, hand stereotypy, preference for routine* and *repetitive phrases/signing* were all more common in the DS+ASD group, albeit with marginal significance). *Tidying, completing behaviour* and *restricted conversation* were also identified as marginally more common in the DS+ASD group at the 'clinical' level (Table 9.6).

[33] The *Total Repetitive Behaviour* scale was transformed using the positive square root in order to adhere to the homogeneity of variance assumption for t-tests.

[34] Comparisons between the "consistent" groups indicated significant differences on the aforementioned scales with the addition of *restricted preferences* (z=3.52, **p<.001**, Cliff's d=.77), and marginal differences were seen in *compulsive behaviour* (z=2.46, **p<.05**, Cliff's d=.48), and *insistence on sameness* (z=2.62, **p<.05**, Cliff's d=.50).

Table 9.5 Median scores, inter-quartile ranges and group differences on the RBQ subscales

RBQ subscale	Group	Median	IQR	Group difference
Stereotyped behaviour	DS+ASD	6.0	0.0-10.0	
	DS-only	0.0	0.0-4.0	z=3.03, **p<.005**, Cliff's d=.48
Compulsive behaviour	DS+ASD	3.5	0.0-8.5	
	DS-only	2.0	0.0-4.5	z=1.29, p=.20, Cliff's d=.21
Restricted preferences*	DS+ASD	3.0	0.0-4.0	
	DS-only	1.5	0.0-3.0	z=1.34, p=.18, Cliff's d=.24
Insistence on sameness	DS+ASD	3.5	0.0-6.3	
	DS-only	0.5	0.0-2.3	z=1.62, p=.10, Cliff's d=.26
Repetitive speech*	DS+ASD	4.0	0.0-7.0	
	DS-only	2.0	0.0-3.0	z=2.14, **p<.05**, Cliff's d=.37

*Analysis only included participants who were able to *'talk using short phrases or sentences'* (SCQ Q1)

Table 9.6 Percentage of children scoring above item level clinical cut-off scores on the RBQ, and group differences, for the DS+ASD and DS-only groups

	Group		Fisher's exact p value
	DS+ASD	DS-only	
Stereotyped Behaviour			
Q1 Object stereotypy	52.17	23.08	**<.05**
Q2 Body stereotypy	43.48	11.11	**<.05**
Q3 Hand stereotypy	47.83	14.81	**<.05**
Compulsive behaviour			
Q4 Cleaning	0.00	0.00	**
Q5 Tidying	17.39	0.00	**<.05**
Q6 Hoarding	0.00	0.00	**
Q7 Organising objects	8.70	3.70	ns
Q12 Rituals	9.09	0.00	ns
Q16 Lining up objects	22.73	15.38	ns
Q18 Completing behaviour	40.90	11.54	**<.05**
Q19 Spotless behaviour	9.09	3.85	ns
Restricted preferences			
Q8 Attachment to people	30.43	11.11	ns
Q10 Attachment to objects	34.78	11.11	ns
Q13 Restricted conversation*	23.08	0.00	**<.05**
Insistence on sameness			
Q15 Preference for routine	50.00	15.38	**<.05**
Q17 Just right behaviour	27.27	15.38	ns
Repetitive speech			
Q9 Repetitive questions*	35.71	29.17	ns
Q11 Repetitive phrases/signing	36.36	7.69	**<.05**
Q14 Echolalia*	23.08	4.35	ns

*Analysis only included participants who were able to *'talk using short phrases or sentences'* (SCQ Q1)
**Unable to conduct analysis due to zero scores

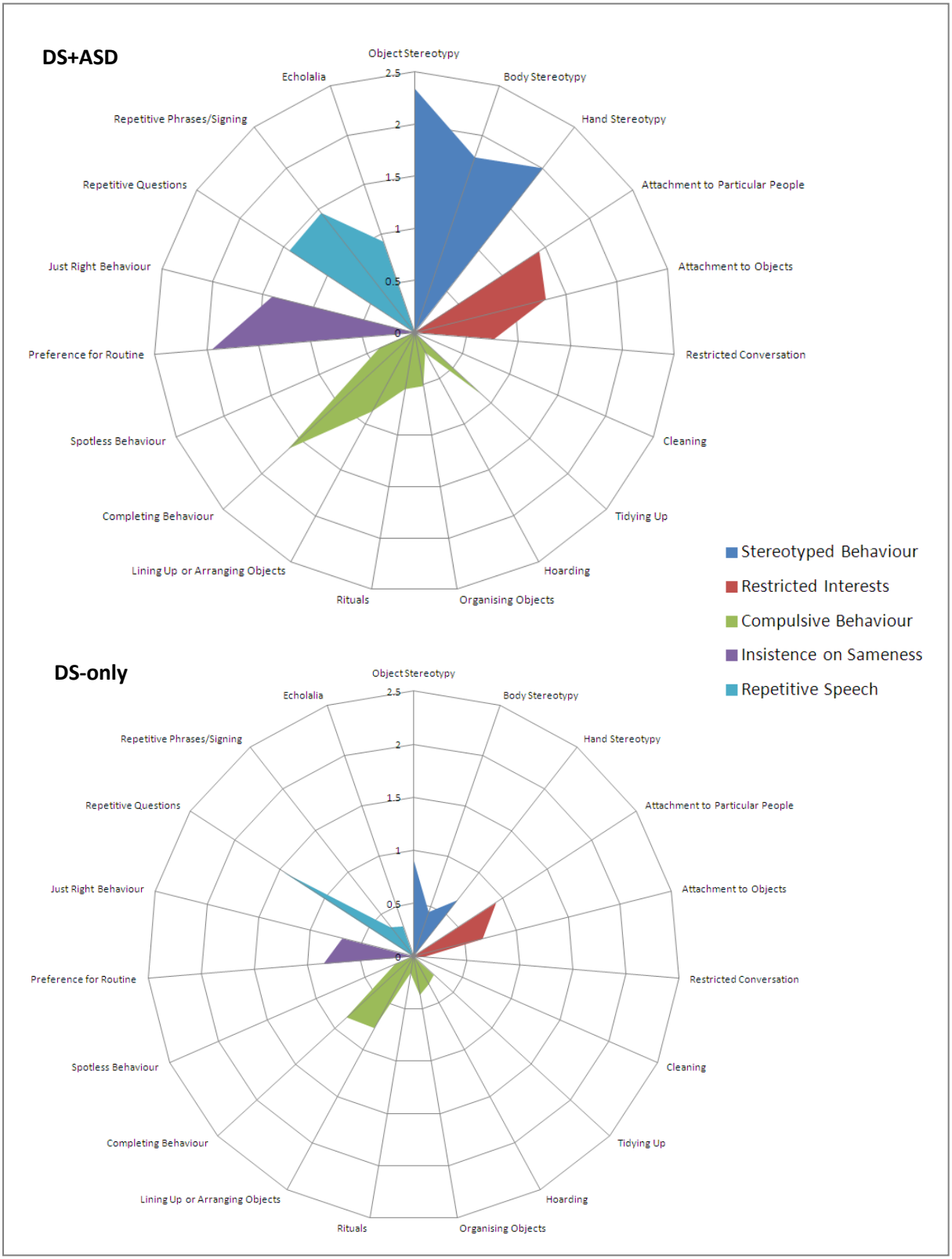

Figure 9.5 Mean item level scores on the RBQ for the DS+ASD and DS-only groups.

Mean scores reported due to uninformative nature of median scores.

Functions of challenging behaviour

Parents were asked to complete the questionnaire about the behaviour their child displayed which they found "most challenging"; 6 parents elected not to complete the questionnaire as they did not find any of their child's behaviour challenging.

According to parent reports, children in the DS+ASD group were more likely to use challenging behaviour for *self-stimulation*, to express *pain or discomfort*, because of a *break in routine* or due to *sensory* issues (e.g. the environment was too bright or noisy). The DS+ASD group were also marginally more likely to use challenging behaviour for *social escape* (i.e. to avoid interaction with another person) (Table 9.7)[35]. These findings support Hypothesis 1.d., with the exception of *pain / discomfort* which was an unexpected finding.

Table 9.7 Median scores, inter-quartile ranges and group differences on the QABF-M

Behavioural function	Group	Median	IQR	Group difference
Attention	DS+ASD	4.0	1.0-9.0	
	DS-only	3.0	2.0-7.0	z=.50, p=.62, Cliff's d=.09
Task escape	DS+ASD	9.0	6.5-12.0	
	DS-only	8.0	3.0-10.0	z=1.49, p=.14, Cliff's d=.26
Self-stimulation	DS+ASD	9.0	3.5-12.0	
	DS-only	1.0	0.0-3.0	z=3.91, **p<.001**, Cliff's d=.68
Pain/discomfort	DS+ASD	5.0	2.0-8.0	
	DS-only	2.0	0.0-3.0	z=2.79, **p<.01**, Cliff's d=.48
Tangibles	DS+ASD	6.0	2.0-10.0	
	DS-only	4.0	2.0-8.0	z=1.03, p=.31, Cliff's d=.18
Sensory	DS+ASD	6.0	2.5-8.8	
	DS-only	1.0	0.0-3.0	z=3.48, **p<.005**, Cliff's d=.61
Break in routine	DS+ASD	7.0	3.7-11.0	
	DS-only	3.0	0.0-6.0	z=2.72, **p<.01**, Cliff's d=.48
Social escape	DS+ASD	8.0	3.0-9.5	
	DS-only	4.0	2.0-6.0	z=2.02, **p<.05**, Cliff's d=.35

[35] Comparisons between the "consistent" groups indicated significant differences on the aforementioned functions, with the addition of a marginal difference in *task escape* (z=2.34, **p<.05**, Cliff's d=.47).

Section 9.2.3 Educational placements and challenging behaviour at school

Research question 3: What are the differences between the DS+ASD group and the DS-only group with respect to:

a.) educational placements

b.) challenging behaviour at school?

Educational placements

Based on information provided by the schools, the type of school attended by each child was identified (e.g. mainstream school / special school). Some children attended both mainstream and special schools (i.e. a few days a week at each). One child was home schooled. Data were analysed in age brackets (i.e. 8-11 years and 12-17 years) to reflect the primary and secondary format of education in the UK (see Figure 9.6 and Figure 9.7).

As predicted in Hypothesis 1.e., the proportion of DS+ASD children in specialist versus mainstream schools (children in other forms of education were excluded[36]) was higher than in the DS-only group (with marginal significance) for both the 8-11 year old (Fisher's exact, **p<.05**) and the 12-17 year old subgroups (Fisher's exact, **p<.05**).

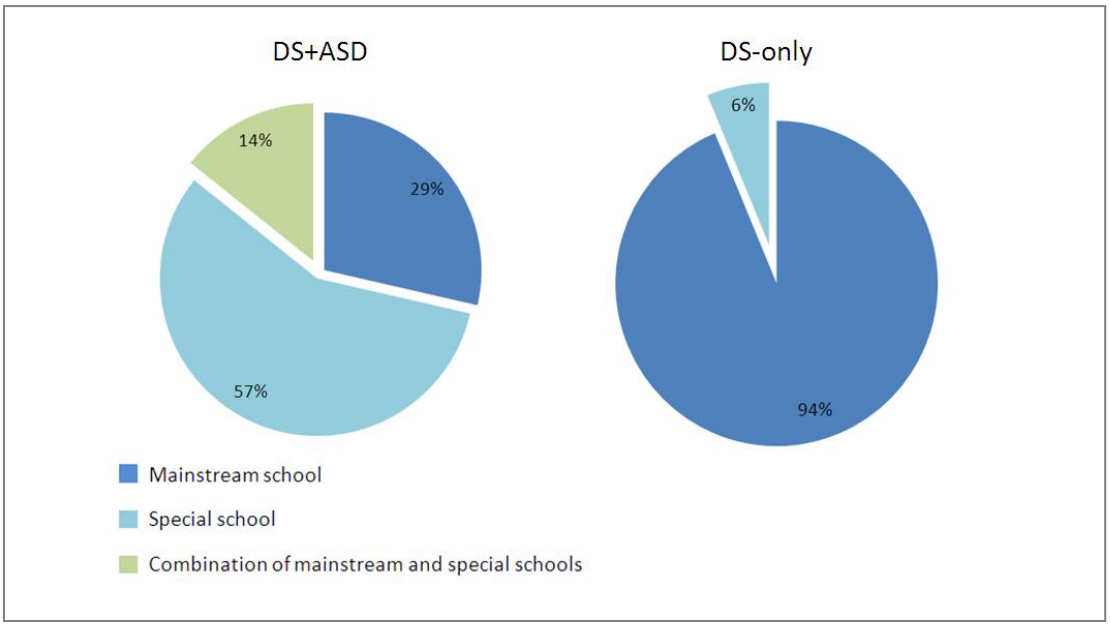

Figure 9.6 The proportion of 8-11 year old children in mainstream, special or combined education in the DS+ASD and DS-only groups

[36] Three children were excluded from the 8-11 year old bracket analysis; 1 child was excluded from the 12-17 year old bracket.

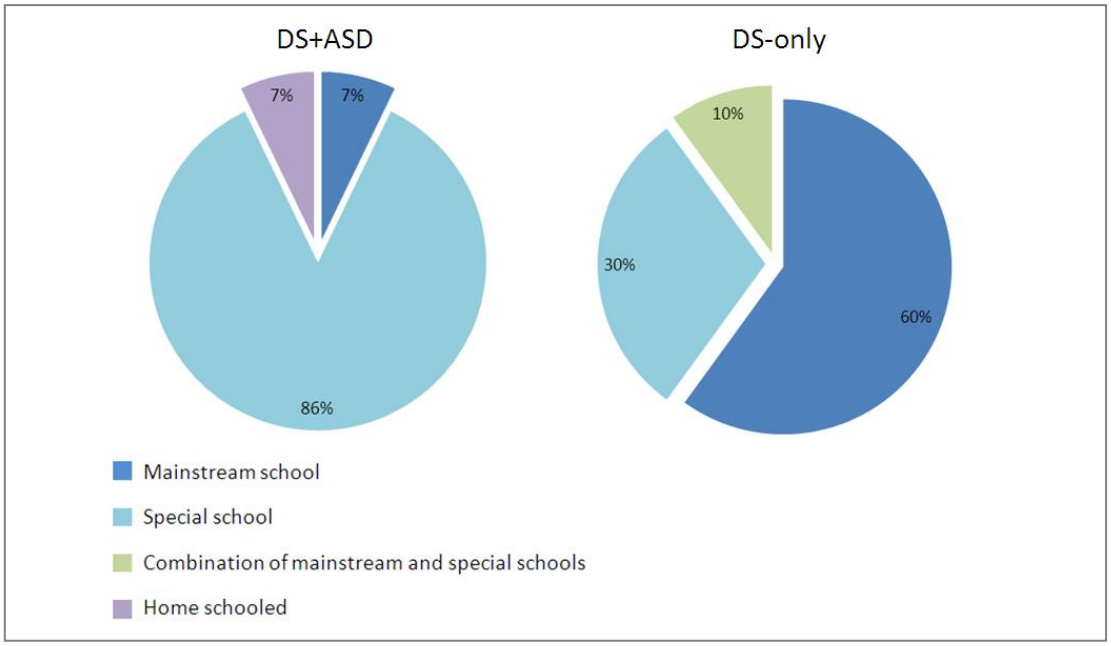

Figure 9.7 The proportion of 12-17 year old children in mainstream, special, home or combined education in the DS+ASD and DS-only groups

Challenging behaviour at school

As predicted in Hypothesis 1.f. (and illustrated in the following sections), children in the DS+ASD group were also more likely to be reported as showing challenging behaviours in school.

Developmental Behaviour Checklist-Teacher Report (DBC-T)

Children in the DS+ASD group scored higher, on average, than the DS-only group for *total behaviour problems* (z=4.74, **p<.001**, Cliff's d=.84) and on the *disruptive*, *self-absorbed* and *communication disturbance* and *anxiety* subscales (see Figure 9.8)[37].

[37] Data missing for 6 children

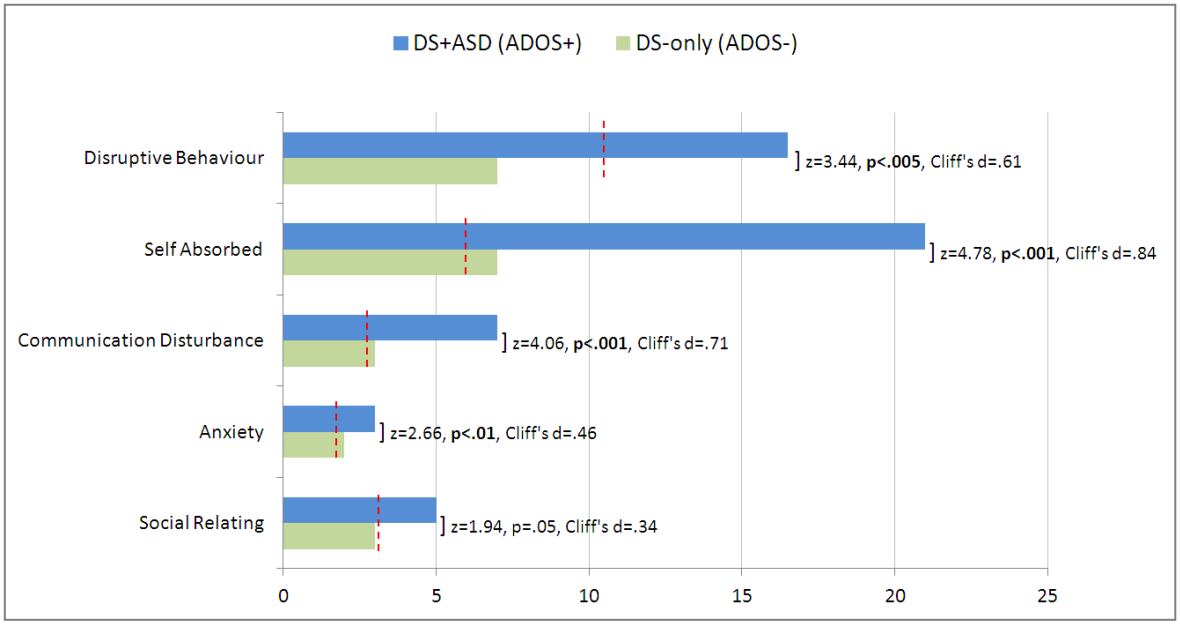

Figure 9.8 Median scores for the DS+ASD and DS-only groups on the DBC-T subdomains (Red dashed lines indicate mean scores for individuals with a mild intellectual disability (IQ 50-70), as outlined in the DBC manual; Einfeld & Tonge, 2002)

Natural observation

During the natural observation session children in the DS+ASD group tended to show more stereotyped behaviours than children in the DS-only group (see Table 9.8) [38].
In the subsamples of children who *did* display the challenging behaviours, the median percentage of the observation period (i.e. 1.5 hours per child) during which the child engaged in the behaviour was compared between the DS+ASD and DS-only groups (see Table 9.9). A group difference (of marginal significance) was seen in the amount of time spent engaging in stereotyped behaviour, with children in the DS+ASD group engaging in the behaviour for longer.

The observation period was then stratified in terms of the situational setting (i.e. *group* / *1-to-1* / *play*) and the median percentage of time spent engaging in the behaviours was assessed for the DS+ASD and DS-only groups (only including those children who displayed the challenging behaviours). A group difference was seen in the amount of time spent engaging in stereotyped behaviour during *play* (Mann Whitney z=3.36, **p<.001**, Cliff's d=.91), with children in the DS+ASD group engaging in the behaviour for longer. No other differences were identified across the remaining behaviours and settings (see Appendix C for outcomes).

[38] Group differences remained the same when the "consistent" groups were compared.

Table 9.8 Percentage of children in the DS+ASD and DS-only groups who demonstrated challenging behaviour during the natural observation

Challenging behaviour	**Group**	**% (n)**	**Group difference**
Self-injury	DS+ASD	18.75 (3)	
	DS-only	11.54 (3)	Fisher's exact, p=.66
Aggression	DS+ASD	50.00 (8)	
	DS-only	26.92 (7)	$\chi^2(1, N=42) = 2.30$, p=.13, φ=.23
Destruction of property	DS+ASD	43.75 (7)	
	DS-only	26.92 (7)	$\chi^2(1, N=42) = 1.26$, p=.26, φ=.17
Stereotyped behaviour	DS+ASD	93.75 (15)	
	DS-only	46.15 (12)	$\chi^2(1, N=42) = 9.77$, **p<.005**, φ=.48
Refusal to comply	DS+ASD	68.75 (11)	
	DS-only	53.85 (14)	$\chi^2(1, N=42) = .91$, p=.34, φ=.15

Table 9.9 Median percentage of observation period that children from the DS+ASD and DS-only groups who demonstrated the challenging behaviours engaged in the behaviours

	DS+ASD			DS-only			Group difference
	n	**Median %**	**IQR[a]**	**n**	**Median %**	**IQR[a]**	
Self-injury[b]	3	0.20	-	3	0.09	-	-
Aggression	8	0.33	0.15-0.68	7	0.20	0.09-1.40	z=.23, p=.87, Cliff's d=.07
Destruction of property	7	0.11	0.09-0.90	7	0.40	0.09-0.93	z=.00, p=1.00, Cliff's d=.00
Stereotyped behaviour	15	6.70	1.85-29.69	12	2.29	0.30-6.15	z=1.98, **p<.05**, Cliff's d=.45
Refusal to comply	11	0.57	0.09-1.30	14	0.54	0.23-1.78	z=-.61, p=.57, Cliff's d=.14

[a]IQR=Inter-quartile range.
[b]Note that the small sample sizes for self-injury prevented an IQR from being calculated and a Mann Whitney U test was deemed inappropriate.

9.3 Associated factors aside from clinical grouping

Research question 4: Are the following factors associated with the outcomes:

a.) Age

b.) Gender

c.) ASD severity

d.) Adaptive behaviour level?

Section 9.3.1 Impact of age

Adaptive behaviour skills (Vineland II)

No hypotheses were made regarding age and adaptive behaviour skills; however, the Vineland II composite score was significantly negatively associated with age (r=-.44, **p<.005**) (see Figure 9.9). That is, older children had relatively worse adaptive behaviour skills. Age demonstrated similar negative associations with the Vineland II subscales (*communication*: r=-.30, **p<.05**; *daily living*: r=-.46, **p<.005**; *socialisation*: r=-.44, **p<.005**). Previous research has suggested that children with DS may alternate between periods of advancement and plateau in the development of skills, including adaptive behaviour (Dykens, Hodapp & Evans, 2006). To examine whether the identified relationship between age and adaptive behaviour skills was stronger at certain points, a series of rolling correlations were conducted (Table 9.10). As Table 9.10 illustrates, the relation of age to the Vineland II composite was strongest in children aged 9 to 15 years; therefore, the line of fit presented in Figure 9.9 represents the relationship within this age bracket.

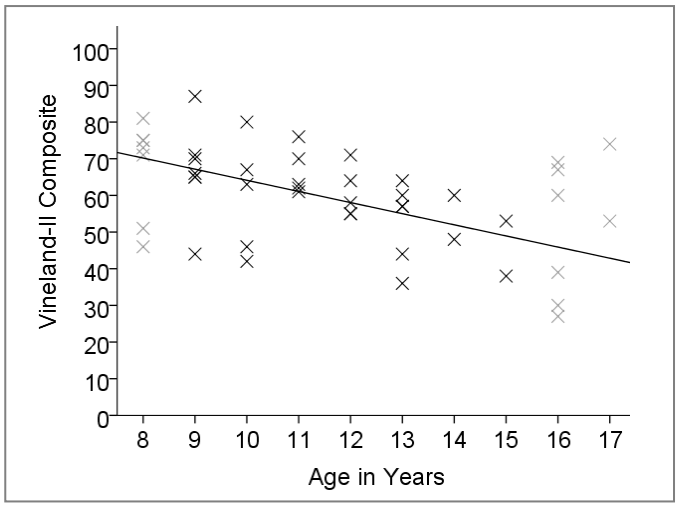

Figure 9.9 Scatter plot of overall adaptive behaviour skills (i.e. Vineland II composite) by age. The line of fit represents the linear relationship for children aged 9 to 15 years.

Table 9.10 Rolling 4 year correlations of chronological age with Vineland II composite

Age range (years)	n	r
8-12	29	.09
9-13	28	**-.45***
10-14	23	**-.36**
11-15	20	**-.66****
12-16	21	-.25
13-17	18	.09

Bold indicates spearman's rho >.30, *significant at the p<.05 level
**significant at the p<.005 level

Challenging behaviour

Although, based on the DBC manual, it was predicted that younger children would be more likely to be self-absorbed and anxious (Hypothesis 2.a.), the only significant relationship was a positive association between age and the DBC-P *communication disturbance* domain (r(48)=.45, **p<.005**). Further (marginally significant) relationships were found between age and *total behaviour problems* (r(48)=.31, **p<.05**) and *social relating* (r(48)=.36, **p<.05**). That is, older children demonstrated greater levels of communication difficulties, as well as more overall behaviour problems and greater levels of social relating problems. On the DBC-T, a marginally significant positive relationship was found between age and *social relating* (r(42)=.31, **p<.05**). Thus, older children were more likely to experience social relating difficulties at school.

Functions of challenging behaviour (i.e. QABF-M)

No hypotheses were made regarding age and functions of challenging behaviour; however, a positive relationship was found between age and using challenging behaviour for *self-stimulation* (r(42)=.41, **p<.01**). That is, older children were more likely to conduct challenging behaviour for the purpose of stimulation.

Section 9.3.2 Impact of gender

The impact of gender was assessed across all measures. Although it was predicted that boys would be more likely to display social relating problems, as measured by the DBC (Hypothesis 2.b.), the only gender effect was identified on the CBQ, where boys were more likely to be reported as demonstrating *physical aggression* than girls ($\chi^2(1, N=50) = 7.56$, **p<.01**, $\varphi = .39$).

Section 9.3.3 Impact of ASD severity

Adaptive behaviour skills (Vineland II)

Controlling for age, partial correlations revealed that ASD severity based on the calibrated severity scale (CSS) was significantly negatively associated with the Vineland II composite score (r=-.55, **p<.001**) (Figure 9.10). That is, as predicted by Hypothesis 2.c., with increasing ASD severity adaptive behaviour skills decreased. Negative associations between ASD severity and the Vineland II subscales were also evident (*communication*: r=-.53, **p<.001**; *daily living*: r=-.53, **p<.001**; *socialisation*: r=-.53, **p<.001**).

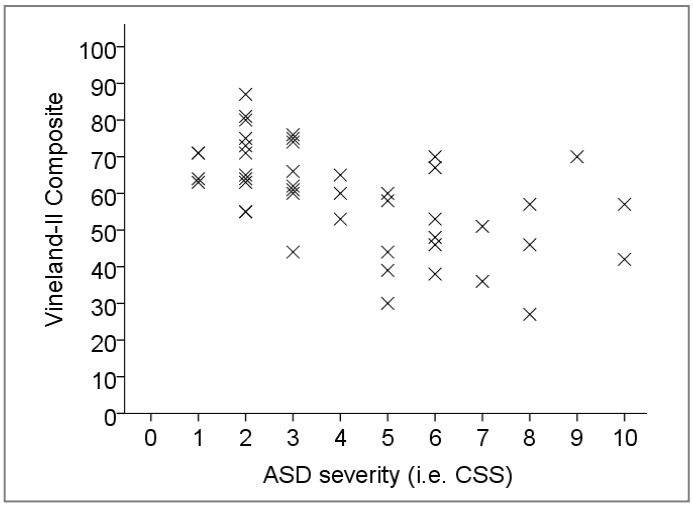

Figure 9.10 Scatter plot of overall adaptive behaviour skills (i.e. Vineland II composite) by ASD severity (i.e. ADOS CSS)

Challenging behaviour

In line with Hypothesis 2.c., positive associations were found between ASD severity and challenging behaviours. Controlling for age, partial correlations revealed that ASD severity (i.e. ADOS CSS) was positively associated with the DBC-P *self absorbed* scale (r(45)=.47, **p<.005**) and marginally positively associated with the *total behaviour problems* scale (r(45)=.30, **p<.05**). On the DBC-T, positive associations were also found on the *total behaviour problems* (r(39)=.65, **p<.001**) and *self-absorbed* (r(39)=.70, **p<.001**) scales, with the addition of the *communication disturbance* scale (r(39)=.54, **p<.001**), and the *disruptive behaviour* scale (r(39)=.39, **p<.05**) at a marginal level.

Section 9.3.4 Impact of adaptive behaviour level

Corresponding to Hypothesis 2.d., regression analysis revealed that the overall adaptive behaviour level (i.e. Vineland II composite) contributed substantially to the ADOS-G scores, accounting for 49% of variability in the Social Affect domain score, 29% of the variability in the Restricted and Repetitive Behaviour domain and 53% of variability in the total score (see Table 9.11).

Table 9.11 Regression analyses evaluating the amount of variance in ADOS-G outcomes explained by adaptive behaviour level (i.e. Vineland II composite)

ADOS-G domain	β	p	R^2	SE of estimate
Social Affect	-.70	<.001	.49	3.99
Restricted and Repetitive Behaviour	-.54	<.001	.29	1.71
Total score	-.73	<.001	.53	4.73

9.4 Factors that affect attendance at a special school

Research question 5: What factors affect whether or not a child attends a special needs school?

Regression analysis (evaluating the effect of adaptive behaviour, behaviour problems and ASD severity) determined that adaptive behaviour was the main factor influencing attendance at a special school (see Appendix C for group comparison and regression analysis outputs; see Chapter 8, Section 8.7 for information on the statistical method and the selection of factors).

Path analysis produced a model which represented a direct effect of total behaviour problems (DBC-T) and ASD severity (ADOS CSS) on adaptive behaviour (Vineland II composite), a direct effect of adaptive behaviour on attendance at a special school, and thus an indirect effect of behaviour problems and ASD severity on attendance at a special school (see Figure 9.11; see Chapter 8, Section 8.7 for the basis of the path analysis). The comparative fit index (.95) suggested that the model was a good fit (as the value approaches 1 the goodness of fit improves).

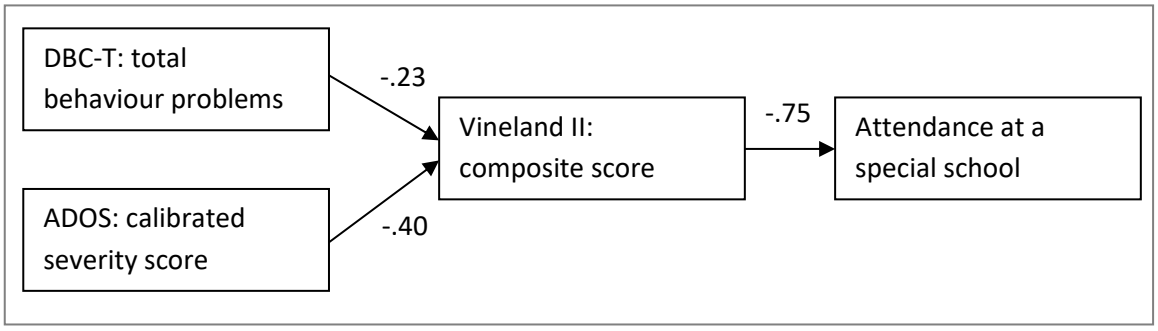

Figure 9.11 Path analysis model exploring the causal relationships between behaviour problems, ASD severity, adaptive behaviour skills and attendance at a special school[39].
Standardised regression coefficients (i.e. Beta) are displayed.

9.5 Differences in parent and teacher reports of challenging behaviour

Research question 6: Are there differences in parent reports and teacher reports of challenging behaviour?

Intra-class correlations (ICC) between parent ratings and teacher ratings on the DBC are displayed in Table 9.12. Good agreement was only seen on the *self-absorbed* subscale (see Chapter 8, Section 8.7 for details on interpretation). Figure 9.12 portrays the mean ratings given by parents and teachers across the whole sample (parent n=50, teacher n=44).

Table 9.12 Intra-class correlations between parent and teacher ratings on the DBC

DBC Scale	ICC	95% CI
Disruptive behaviour (DB)	.64	.34-.81
Self absorbed (SA)	.85	.72-.92
Communication disturbance (CD)	.54	.18-.75
Anxiety (A)	.45	.03-.69
Social relating (SR)	.62	.31-.79
Total behaviour problems (TBP)	.64	.35-.80

[39] Note that a higher score on the DBC-T total behaviour problems scale indicates greater severity of behavioural disturbance, and a higher score on the ADOS CSS indicates greater severity of ASD symptoms. Whereas, a lower score on the Vineland II indicates greater severity of adaptive behaviour problems. For the analysis attendance at a special school was coded with a value of 1, and attendance at a mainstream school was coded with a value of 0.

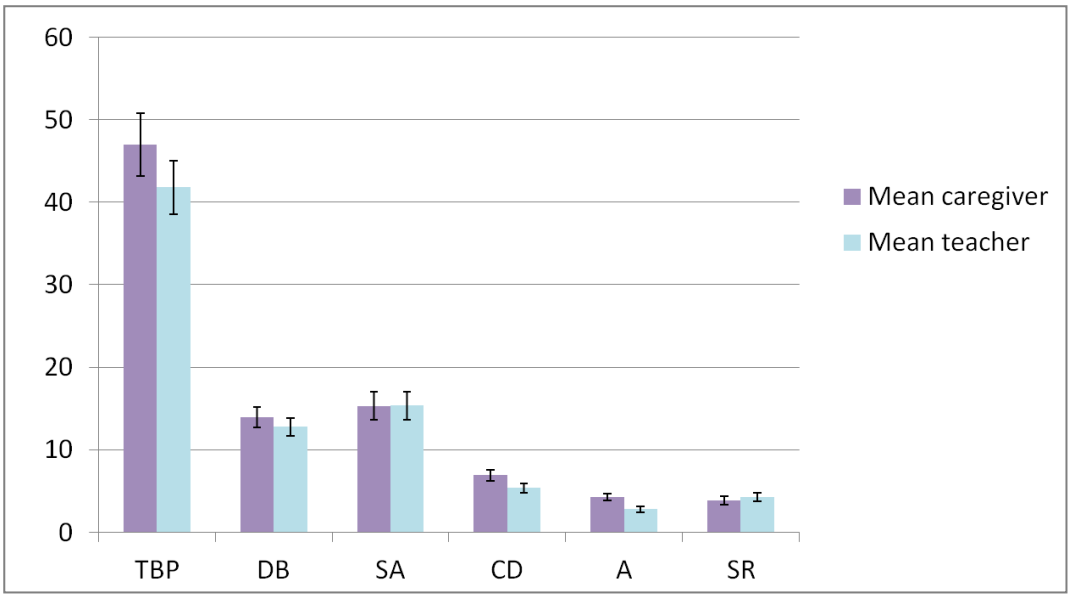

Figure 9.12 Mean parent and teacher ratings on the DBC

Error bars represent standard error of the mean

9.6 Individual differences among children in the DS+ASD group

Research question 7: What is the range of individual differences within the DS+ASD group?

Adaptive behaviour

A summary of the DS+ASD group scores on the Vineland II (see Figure 9.13) reveals that all of the children scored in the 'low' range for their overall adaptive behaviour skills (i.e. Vineland II composite score). Seventy-five percent of the children scored ≤ 60, demonstrating a general low level of ability in this group. Consideration of the subscales (*communication, daily living skills* and *socialisation*) highlighted that the most variability within the group was in communication skills (Mean Absolute Deviation (MAD) =11.59) and the group varied the least in socialisation skills (MAD=9.02). The greatest overall range (i.e. highest score – lowest score) was seen on the *daily living* subscale, indicating that the DS+ASD group included extreme cases of children who managed personal and domestic tasks with some independence as well as children who were unable to function without a great deal of daily support.

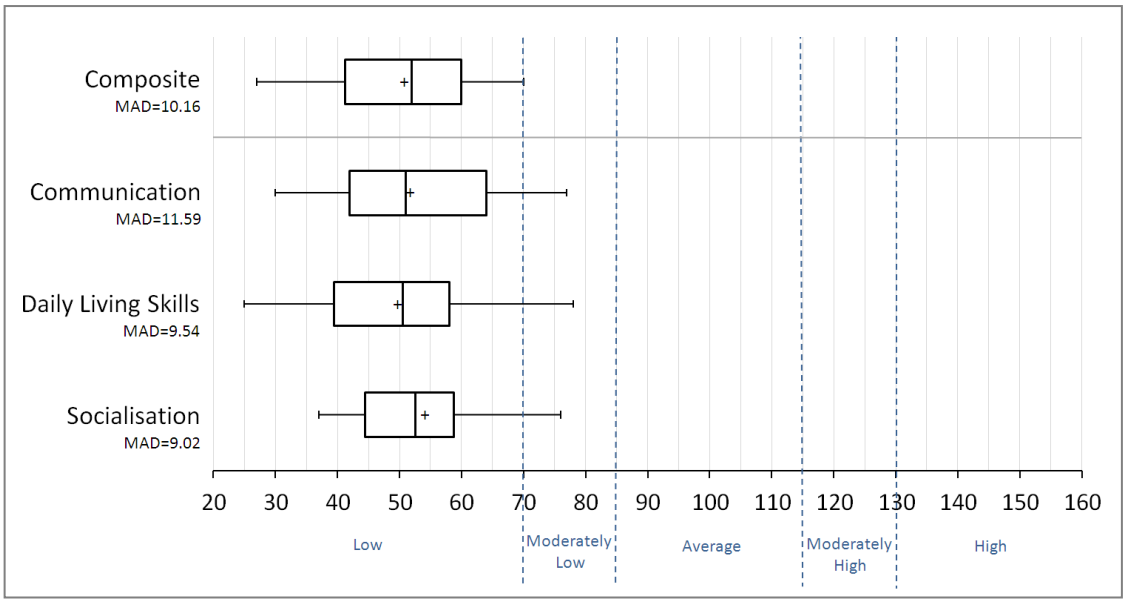

Figure 9.13 Distribution of the DS+ASD group scores on the Vineland II

Mean scores indicated by a plus sign. MAD=Mean Absolute Deviation. Adaptive level descriptions in blue[40]

ASD severity

Since all children in the DS+ASD group had severity scores ≥4, the potential range of scores was restricted (see Figure 9.14). However, the overall range (i.e. highest score – lowest score) was as large as it could be, indicating that the group included extreme cases of both profound autism and mild ASD. Half of the children scored between 5 and 8, the median CSS was 6 and the Median Absolute Deviation (MAD)[41] was 1.35, indicating that most children were in the 'moderate' range.

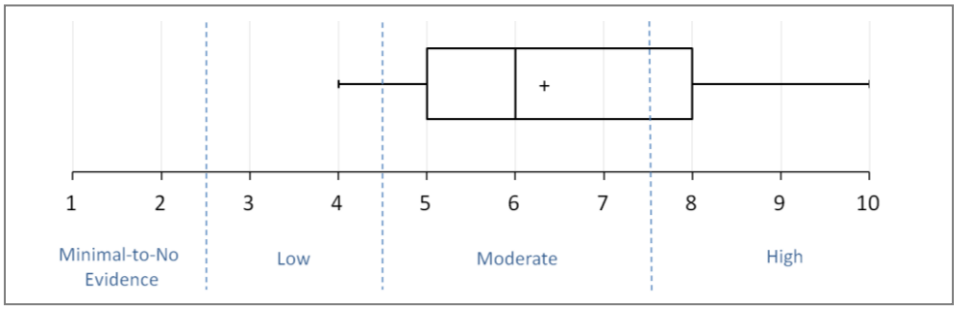

Figure 9.14 Distribution of the DS+ASD group scores on the ADOS CSS

Mean score indicated by a plus sign. Autism spectrum level descriptions in blue[42]

[40] Adaptive level descriptions taken from the Vineland II manual (Sparrow et al.,2005); the descriptions express in words the approximate distance of the score range from the age-group mean.
[41] Median (opposed to Mean) Absolute Deviation was calculated because the data were skewed.
[42] Autism spectrum level descriptions taken from ADOS-2 administration form (Rutter et al., 2012).

Repetitive behaviour

Out of a possible total repetitive behaviour score of 95, the highest score within the DS+ASD group was 49. The overall range (i.e. highest score – lowest score) was large with some children in the DS+ASD group reportedly showing no repetitive behaviours at all. Comparison of variability across the subscales (*stereotyped behaviour, compulsive behaviour, restricted preferences, insistence on sameness* and *repetitive speech*) was difficult given that each subscale included a different number of questions and thus yielded a different total score. However, inspection of the box plots and the MAD values relative to the scale totals (see Figure 9.15), indicated that the greatest variability was on the insistence on sameness and stereotyped behaviour scales. The overall range (i.e. highest score – lowest score) on the repetitive speech scale nearly equated the total scale value (range=14, total score=15), suggesting that the DS+ASD group included extreme cases of children who reportedly engaged in an excessive amount of repetitive speech, as well as several children who were reported as using none (lower quartile=0).

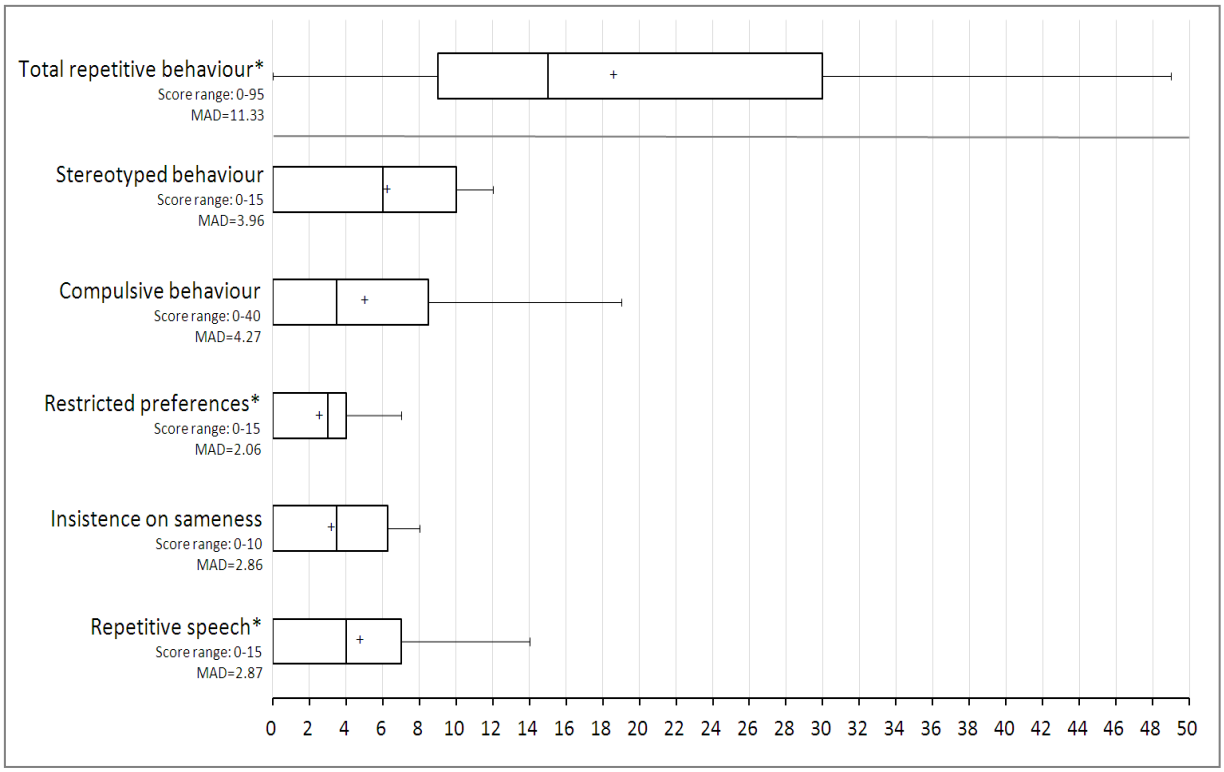

Figure 9.15 Distribution of the DS+ASD group scores on the RBQ

*Analysis only included participants who were able to *'talk using short phrases or sentences'* (SCQ Q1)

Mean scores indicated by a plus sign. MAD=Median Absolute Deviation[43]

[43] Median (opposed to Mean) Absolute Deviation was calculated because the data were skewed for several of the scales.

Behaviour problems

For the purpose of comparison across the scales, the DBC-P scores of the DS+ASD group were transformed into percentiles according to instructions in the DBC manual (Einfeld & Tonge, 2002). A summary of the data (see Figure 9.16) highlights that a considerable number of children in the DS+ASD group scored above the clinical cut-off (score=46, percentile=58) and thus would be classified as having 'major behavioural/emotional disturbance' (Einfeld & Tonge, 2002). However, the overall range (i.e. highest score – lowest score) indicates that the group included extreme cases of children who reportedly demonstrated profound behavioural issues as well as children who reportedly demonstrated very few behavioural problems. Consideration of the subscales (*disruptive behaviour, self-absorbed, communication disturbance, anxiety* and *social relating*) highlighted that the most variability within the group was in social relating (MAD=29.04) and the group varied the least in disruptive behaviour (MAD=20.09).

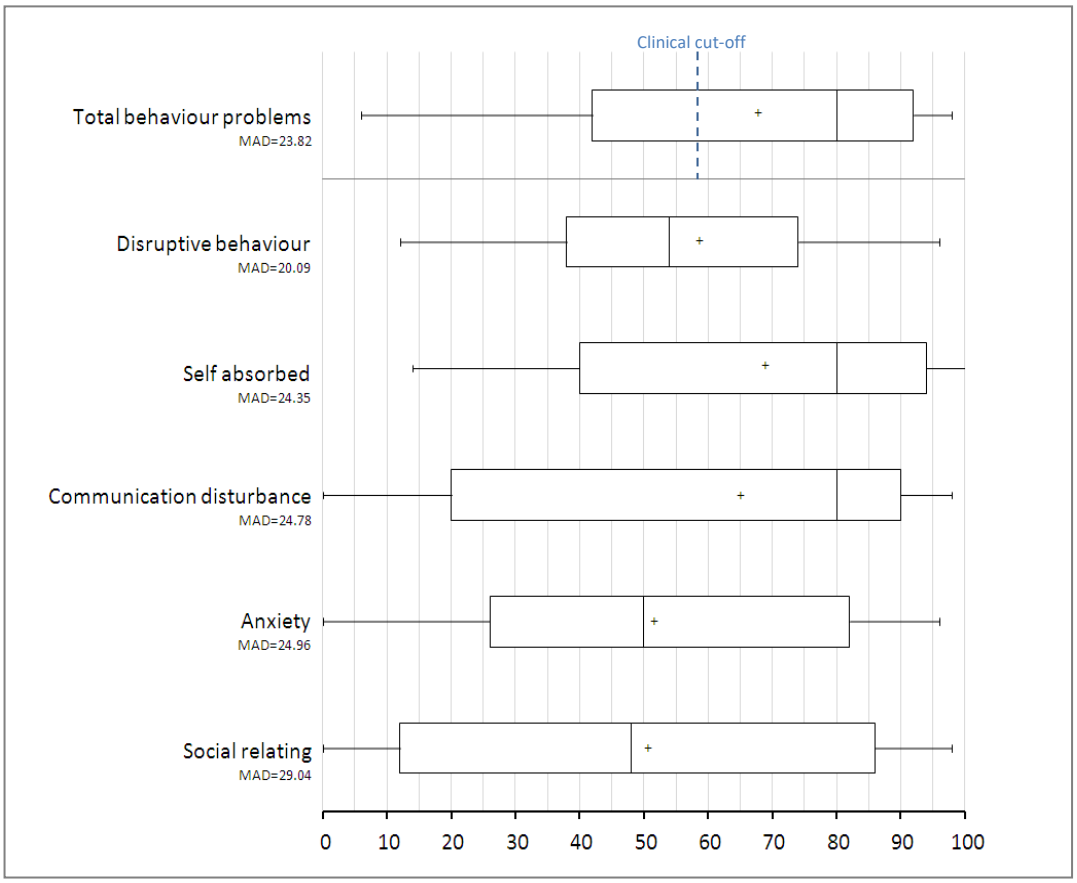

Figure 9.16 Distribution of the DS+ASD group across the standardised percentiles for the DBC-P. Mean scores indicated by a plus sign. MAD=Median Absolute Deviation[44]

[44] Median (opposed to Mean) Absolute Deviation was calculated because the data were skewed for several of the scales.

Chapter 10: Group study discussion

Outline:
This chapter provides discussion on the findings of the group study in the context of previous research. The main findings are presented in boxes throughout the discussion. Limitations of the study are also reported.

10.1 Group characteristics

When conducting research of this kind the direct assessment of participants (as opposed to reliance on report measures) allows for consistent evaluation across the whole sample. For the present study, when assessing the presence of autism spectrum disorder (ASD) characteristics, it was important to utilise a measure that was independent of intelligence quotient (IQ) and demonstrated balanced sensitivity and specificity in relatively low functioning children; these are qualities that have been verified for the Autism Diagnostic Observation Schedule (ADOS) revised algorithms (de Bildt et al., 2009). Therefore, it was justified to structure the recruited groups, not on the basis of their SCQ scores as had been initially planned, but according to the ADOS-G (with revised algorithms). The restructuring of the groups resulted in small and non-significant differences in age and gender proportion as indicated by small effect sizes (non-significant p values). Age and gender effects were investigated alongside other possible associated factors aside from the clinical grouping (see Section 10.3 for discussion).

10.2 Group comparisons

Section 10.2.1 Adaptive behaviour and autism profiles

Adaptive behaviour

Compared with children with Down syndrome (DS) only, children in the DS+ASD group:

- had lower Vineland II composite scores
- were more impaired on all 3 subscales (*communication*, *daily living*, and *socialisation*)

The relative impairment in Vineland II scores among the DS+ASD group supports previous findings (Molloy et al., 2009). Mean scores were also similar to those reported by Molly et al. (2009) (i.e. DS+ASD~50; DS-only~70 across all scales). However, the area in

which the DS+ASD group seemed to be most impaired was in communication skills, whereas Molloy et al. (2009) found the greatest difference in socialisation.

Utilising mean Vineland II scores from a group of 9-17 year old children with ASD (Kanne et al., 2011), it appears that children in the DS-only group demonstrate a similar level of ability to children with idiopathic ASD (Figure 9.1). However, closer inspection of the adaptive behaviour profiles highlights a relative weakness in daily living skills in the DS-only group, compared to a relative strength in the ASD group. Given that communication and socialisation deficits are inherent in ASD, the finding that daily living skills are relatively less impaired is not unexpected. It appears as though the co-occurrence of DS and ASD, both of which independently negatively affect adaptive behaviour skills, results in a cumulative impact.

Figure 9.1 demonstrates clearly how the functional ability level of the DS+ASD group was lower than that of an idiopathic ASD group. Although not surprising given previous findings, it raises the question of whether or not the increased presentation of ASD symptomatology is due to the low cognitive ability in this group. IQ measures were not utilised in the present study due to the difficulty of administration in this group (see Chapter 13 for further discussion), but taking the Vineland II as a proxy measure of cognitive ability suggests that the DS+ASD were very low functioning. The relationship between functional ability and ASD symptom severity is considered further in Section 10.3.

Autism profiles

Compared with children with DS only, children in the DS+ASD group:

- had higher total and domain level ADOS-G scores
- were significantly more impaired on the following items: *overall level of language, gestures, eye contact, facial expressions, shared enjoyment, quality of social overtures, imagination/creativity, sensory interests, hand stereotypies, excessive interests,* and *aggression*

The higher scores across the ADOS-G domains produced by the DS+ASD group were expected. However, the item level analysis highlighted subtle differences in the presentation of certain ASD characteristics across the groups that were *not* statistically different (i.e. *echolalia, stereotyped phrases, self-injury* and *anxiety*). Group differences in *intonation* and *overactivity* only achieved marginal significance.

The results on the *echolalia* item support the findings from the RBQ clinical cut-off analysis (Table 9.6), with the DS+ASD group showing a higher rate than the DS-only group but with *no* significant group difference. A similar finding was reported in a paper comparing children with idiopathic ASD with children with Cornelia de Lange (CdLS) syndrome (Moss et al., 2012). Therefore, despite the presence of echolalia in the ASD phenotype, it is not the most prominent characteristic of ASD and appears to be shared by other syndromes.

The subtle group difference in use of *stereotyped phrases* supports the findings from the odds ratio analyses in the questionnaire survey of England and Wales (see Figure 7.1). The term *stereotyped phrases* focuses on the 'quality' of phrases used by the child (opposed to repetitive nature, as measured by the *repetitive phrases/signing* item on the RBQ - for which a group difference *was* identified). For the *stereotyped phrases* item the phrases may be intended meaningfully, and can be appropriate to the conversation at some level, however they appear 'odd' with an unusual use of words, formation of utterance or a consistent intonation pattern. The DS+ASD group in the present study showed a similar level of impairment to the idiopathic ASD group in the CdLS paper (Moss et al., 2012). When the ASD group was compared with the CdLS group a significant difference was found. Therefore, it can be inferred that the lack of a group difference in the present study was due to the higher rate of stereotyped phrases in the DS-only group (compared with the CdLS group)[45]. Children with DS show greater levels of phonological errors than children with other developmental disorders (Barnes et al., 2009), so perhaps syntactic simplification and the utilisation of learnt key phrases is a successful strategy for children with DS.

The lack of a group difference in *self-injury* is due to zero ratings of the behaviour. This contradicts findings from the CBQ which indicated a higher rate of the behaviour in the DS+ASD group (see Table 9.4). The lack of observed self-injury during the ADOS-G assessments may be due to the limited time period not allowing enough opportunity for the child to exhibit the behaviour.

The similar level of *anxiety* seen in the DS+ASD and DS-only groups supports the findings from the DBC-P (see Figure 9.4), but not those produced by the DBC-T (see Figure 9.8), perhaps indicating that environmental factors and/or disparity in interpretation are playing a part.

[45] The majority of individuals with Cornelia de Lange syndrome have a mild to moderate intellectual disability, making them a fair comparison group for Down syndrome with regard to cognitive ability – an important factor to consider when comparing linguistic behaviours such as stereotyped phrases.

Section 10.2.2 Challenging behaviour from the parent perspective

Summary of findings from the DBC-P

Compared with children with DS only, children in the DS+ASD group:

- scored higher for *total behaviour problems* and *self-absorption*
- scored marginally higher for *communication disturbance* and *social relating difficulties*

Comparison of the "consistent" groups (i.e. SCQ+ADOS ratings in agreement) resulted in significant differences on *all* scales, including the *disruptive behaviour* and *anxiety* scales

Interpretation of findings from the DBC-P

As expected, the DBC-P indicated higher levels of self-absorption in the DS+ASD group, compared with the DS-only group. This behavioural characteristic (as well as communication disturbance and social relating difficulties which were found to be marginally more common in the DS+ASD group) is inherent in the ASD phenotype and used as a clinical indicator of the presence of the disorder (DSM-V; see Chapter 2, Section 2.2.1). Previous studies support these findings. Hepburn and MacLean (2009) found that higher levels of self-absorbed and social relating problems were reported on the DBC-P for children with DS and co-morbid ASD than children with DS only. Several studies have indicated an increased rate of stereotyped behaviours in individuals with DS and ASD (Capone et al., 2005; Carter et al., 2007; Moss et al., 2013b), which form part of the *self-absorbed* scale on the DBC (item examples include: *'Flicks, taps, twirls objects repeatedly'*; *'repeated movements of hands, body, head or face…'*). Several forms of communication disturbance such as poorer language skills (Molloy et al., 2009), repetitive language (Moss et al., 2013b) and inappropriate speech (Capone et al., 2005) have previously been identified. Social withdrawal, which can be aligned with social relating difficulties, has also been highlighted (Carter et al., 2007).

Contrary to previous reports of high levels of disruptive (Capone & Kaufmann, 2011) and anxious (Carter et al., 2007) behaviours in individuals with DS and co-morbid ASD, in the present sample there were *no* overall group differences in levels of disruptive and anxious behaviour. However, when analysis was restricted to the "consistent" groups only, significant differences were found on all subdomains including *disruptive behaviour* and *anxiety*, albeit with small effect sizes (Cliff's d= .27 and .25 respectively). It is possible that the SCQ screening efficacy is affected by levels of disruptive and anxious behaviours (see Chapter 11 for further discussion).

Relative to the mean scores for individuals with a mild intellectual disability (ID) (IQ 50-70)[46] (Einfeld & Tonge, 2002), the DS+ASD group scored high for self-absorption and communication disturbance which fits with the fact that these are core aspects of ASD (see Chapter 2, Section 2.2.1). Relative to the mild ID scores, the DS-only group scored low on all DBC-P behaviour scales, with the exception of the *anxiety* scale on which both groups (DS+ASD and DS-only) scored in line with the mild ID average. These relative strengths, particularly in *social relating*, seem to be typical of the DS behavioural phenotype as described in previous literature (e.g. Fidler & Nade, 2007).

Summary of findings from the CBQ

Compared with children with DS only, children in the DS+ASD group:

- were more likely to be reported as showing *self-injury, physical aggression, destruction of property* and *stereotyped behaviour*
- needed more frequent physical contact, prevention or restraint in response to *refusal to comply*

Comparison of the "consistent" groups resulted in significant differences on *all* challenging behaviours, including *refusal to comply*

Interpretation of findings from the CBQ

As expected, the CBQ indicated higher rates of *stereotyped behaviour* in the DS+ASD group, compared with the DS-only group. Previous studies support this finding (Capone et al., 2005; Carter et al., 2007; Moss et al., 2013b). The higher rate of *self-injury* is also a replication of previous findings (Moss et al., 2013b).

However, the increased rates of *physical aggression* and *destruction of property* contest previous outcomes. Moss et al. (2013b) utilised the same measure (CBQ) in a DS/ DS+ASD/ ASD group comparison. Despite the DS+ASD group demonstrating higher rates of *physical aggression* and marginally higher rates of *property destruction* than the DS group, these differences were *not* significant. The discrepancy between findings may be due to sample characteristics given that Moss et al. (2013b) had a much wider age range (4-43 years) and smaller group sizes (n=17).

[46] The comparison with individuals with a *mild* intellectual disability (opposed to *moderate* or *severe*) was determined based on the findings of the Vineland Adaptive Behaviour Scales II (see Chapter 9, Section 9.2.1). The mean scores are indicated on Figure 9.4 by red dashed lines.

Given the reportedly 'stubborn' nature of children with DS (Dykens, 2007), *refusal to comply* was expected to be pervasive across the DS+ASD and DS-only groups. Thus, the absence of a group difference was not surprising. However, this was contradicted when the analysis was run with the "consistent" groups (SCQ+ADOS+ vs. SCQ-ADOS-). Despite this, it is evident that the nature of the refusal is more physical in the DS+ASD group given the need for physical contact, prevention or restraint. Furthermore, a marginally significant finding indicated that the children in the DS+ASD group tended to show the behaviour more often (daily rather than weekly).

Summary of findings from the RBQ

Compared with children with DS only, children in the DS+ASD group:

- were reported to show higher levels of *stereotyped behaviours*
- were more likely to show all forms of stereotyped behaviours (*object, body* and *hand*)

Comparison of the "consistent" groups resulted in significant differences on *all* scales, including the *compulsive behaviour, restricted preferences* and *insistence on sameness* scales

Interpretation of findings from the RBQ

The DS+ASD group was expected to show a greater level of repetitive behaviours because repetitive and restricted behaviours are inherent in the ASD phenotype and are used as clinical indicators of the presence of the disorder (DSM-5; see Chapter 2, Section 2.2.1). Deficits in executive functioning common to ASD, such as impaired cognitive flexibility, have also been linked to the presentation of general repetitive behaviours (Lopez et al., 2005). However, the higher DS+ASD group score on the total RBQ scale was only marginally significant.

The purpose of utilising the RBQ was to consider the specific topographies of repetitive behaviour, to identify whether there are certain repetitive behaviours that are common to DS and co-morbid ASD and others that are not.

At subscale level the DS+ASD group showed significantly higher levels of *stereotyped body movements*. Previous studies support this finding (Capone et al., 2005; Carter et al., 2007; Hepburn & MacLean, 2009; Moss et al., 2013b). Such rhythmical body movements may be providing the children with sensory feedback to help regulate their sensory processing. Hepburn and MacLean (2009) found that children with DS and co-morbid ASD reportedly demonstrated more unusual sensory interests than children with

DS only. There is a widespread belief that sensory symptoms are integral to the ASD phenotype, with the suggestion that up to 95% of children with ASD have sensory processing difficulties (Tomchek & Dunn, 2007). A review of the literature indicated that sensory symptoms are prominent in children with ASD, when compared with typically developing children, and are most likely indicative of hypo-responsiveness (Rogers & Ozonoff, 2006). Although there is a dearth of research into sensory processing in individuals with DS, studies which include participants with DS in generic 'developmental delay' comparison groups indicate a lower rate of abnormal sensory symptoms than individuals with ASD (Baranek et al., 2006). Baranek et al. (2006) found that some children with ASD demonstrated hypo-responsiveness and some demonstrated hyper-responsiveness (a finding that was replicated in children with developmental delay, to a lesser extent in both cases), and that some children with ASD showed fluctuation between hyper- and hypo-responsiveness (a finding that was *not* seen in the developmental delay group). Although it should not be assumed that all repetitive behaviours, such as stereotypy, are linked to sensory stimulation (Cunningham & Schreibman, 2008), Chen et al. (2009) found a significant relationship between the presence of sensory abnormalities and repetitive behaviours. Therefore, sensory processing difficulties may be underlying the increased rates of *stereotyped body movements* in the DS+ASD group.

Although the DS-only group did *not* show any repetitive behaviours to a greater extent than the DS+ASD group, a within-group inspection of the clinical cut-off percentages highlights *repetitive questions* as the most common form of repetitive behaviour (see Table 9.6). The verbal short-term memory deficits reported in individuals with DS (Jarrold et al., 2002) might account for this behaviour.

Group differences (DS+ASD vs. DS-only) in *compulsive behaviour, restricted preferences* and *insistence on sameness* were *not* evident in the first analyses (i.e. ADOS+ vs. ADOS-), and the group difference in *repetitive speech* only had marginal significance. However, analysis of data from the "consistent" groups (i.e. SCQ+ADOS+ vs. SCQ-ADOS-) produced group differences on *all* repetitive behaviour scales (some with marginal significance according to p values but all with large effect sizes). These discrepancies may be due to differences in the sensitivity of the ADOS-G and SCQ to repetitive behaviours (see Chapter 11, Section 11.4, p.178 for further discussion).

Function of challenging behaviour

Compared with children with DS only, children in the DS+ASD group were more likely to use challenging behaviour due to:

a) self stimulation

b) pain or discomfort

c) sensory reasons

d) *break in routine*

Comparison of the *consistent* groups resulted in significant differences on the aforementioned functions, with the addition of *task escape*

The DS+ASD group were expected to be more likely to engage in challenging behaviour for the purpose of *self-stimulation*, for *sensory* reasons, because of a *break in routine* or for *social escape*. These group differences were identified in the present study; however, the group difference in *social escape* only had marginal significance.

The increased likelihood of using challenging behaviour for *self-stimulation* supports the previous finding of higher levels of *stereotyped body movements* in the DS+ASD group and the possible connection to the sensory processing difficulties associated with ASD (see p. 157-158). The need for self-stimulation implies hypo-responsiveness to sensory stimuli; however, the additional identification of *sensory reasons* (i.e. the environment is too bright or noisy) as a function of challenging behaviour in the DS+ASD group implies hyper-responsiveness to sensory stimuli. This provides implied support for Baranek et al. (2006) who found that hyper- and hypo- responsiveness can be experienced and that some individuals fluctuate between both.

The identification of *break in routine* (and *social escape* at a marginally significant level) as a function of challenging behaviour in the DS+ASD group is not surprising given the inclusion of 'inflexible adherence to routines' (and 'absence of interest in peers') in the diagnostic criteria for ASD (DSM-V; see Chapter 2, Section 2.2.1).

The use of challenging behaviour to attain *attention* or *tangibles* was common across both groups (DS+ASD and DS-only). A review of the literature on the causes of challenging behaviour identified *attention* as the most prevalent function (Matson et al., 2011); *tangibles* was less frequent but still identified as a common function. The group difference identified in using challenging behaviour due to *pain or discomfort* was not expected, but could be related to the relatively poor communication skills of the DS+ASD group (see Section 10.2.1).

Section 10.2.3 Educational placements and challenging behaviour at school

School placements

The evaluation of the educational placements of the groups highlighted that children in the DS+ASD group were marginally more likely to attend a special school at primary and secondary level. The adaptive behaviour skills of the children had a direct effect on their school placement, and ASD severity, as well as behaviour problems (although to a lesser extent), had a direct effect on adaptive behaviour skills. This indicates that although a significantly greater number of children in the DS+ASD group attended special schools, the acuteness of a child's ASD characteristics does not in itself influence whether or not the child attends a special school, nor does the presentation of behavioural problems. Instead, the limited level of adaptive functioning, influenced by ASD severity and behaviour problems, is the most important factor.

Summary of findings from the DBC-T

Compared with children with DS only, children in the DS+ASD group:

- reportedly showed higher levels of *total behaviour problems, disruptive behaviour, self-absorption, communication disturbance* and *anxiety*

Comparison of the "consistent" groups resulted in significant differences on *all* scales, including the *social relating* scale

Interpretation of findings from the DBC-T

The identification of group differences on certain DBC subscales (i.e. *disruptive behaviour, social relating* and *anxiety*) differed between parent reports and teacher reports (see Section 10.4 for a discussion of the disparity).

The DBC-T reports of higher levels of disruptive behaviour (Capone & Kaufmann, 2011) and communication disturbance (Capone et al., 2005; Molloy et al., 2009; Moss et al., 2013b) support previous findings. Previous research into levels of anxiety in DS and co-morbid ASD has been mixed (Carter et al., 2007; Dressler et al., 2011). Self-absorption in the DS+ASD group appeared to be pervasive across home and school, supporting previous reports of stereotyped behaviours (Capone et al., 2005; Carter et al., 2007; Moss et al., 2013b) which form part of the *self-absorbed* scale on the DBC.

The mean scores for individuals with a mild ID (IQ 50-70)[47] (Einfeld & Tonge, 2002) appeared lower on the DBC-T than the DBC-P. This shift was disproportionate to that seen in the DS-only group scores which was resultant in the relative strengths of the DS-only group observed on the DBC-P (see Section 9.2.2) disappearing on the DBC-T. The DS+ASD group showed raised levels of certain behaviours on the DBC-T opposed to the DBC-P (i.e. *disruptive behaviour, communication disturbance* and *social relating*). Consequently, the DS+ASD group scored higher than the mild ID mean scores on *every* behaviour scale.

Summary of findings from the natural observation

Compared with children with DS only, children in the DS+ASD group:

- were more likely to be observed carrying out *stereotyped behaviour*
- engaged in *stereotyped behaviour* for longer during 'play' sessions (including only those children who demonstrated stereotyped behaviour)

Interpretation of findings from the natural observation

The fact that more children in the DS+ASD group were observed demonstrating *stereotyped behaviour* than the DS-only group provides ecological validation of the findings of the DBC-P, CBQ, RBQ and DBC-T and previous research studies (Capone et al., 2005; Carter et al., 2007; Moss et al., 2013b) which all indicated raised levels of stereotyped behaviour in this group of children.

The identification of 'play' sessions as a setting in which children in the DS+ASD group tended to engage in stereotyped behaviours for longer (compared with children in the DS-only group who also demonstrated stereotyped behaviour) suggests that for these children a lack of structure in the environment may act as a function of stereotyped behaviour. Caution must be taken when interpreting this finding as sample sizes were dramatically reduced for the analysis. However, the finding provides grounding for future work addressing the function of stereotyped behaviours in children with DS and co-morbid ASD (see Chapter 13, Section 13.5 for further suggestions for future research).

[47] The mean scores are indicated on Figure 9.8 by red dashed lines.

10.3 Associated factors aside from clinical grouping

A temporary plateau in development was noted in overall adaptive skills, aligning with previous work that reports periods of stability between advancements in the development of children with DS (Dykens et al., 2006). Communication disturbance appeared to worsen with age, which is likely due to advancing expectations. Children with DS may hit early milestones (albeit at a delayed rate); however, they may never achieve the later milestones outlined in the Vineland II (e.g. *'listening to an informational talk for at least 30 minutes', 'gives complex instructions to others', 'reads at least two newspaper articles weekly'* and *'writes business letters'*).

The increased likelihood of boys demonstrating physical aggression is supported by a body of work (for a meta-analysis see Cared et al., 2008). The DS+ASD group were more likely to show physical aggression than the DS-only group (see Section 10.2.2). An overrepresentation of males in the DS and co-morbid ASD population has been indicated (based on SCQ screening) (see Chapter 6, Section 6.4.3) and is noted in idiopathic ASD (Fombonne, 2003). Thus, the causation of physical aggression may derive from biological differences pertaining to gender rather than, or perhaps in addition to, the influence of the ASD.

ASD symptom severity was negatively associated with adaptive behaviour skills, which is not surprising given that children with ASD demonstrate relatively low adaptive behaviour skills when compared with typically developing children (Tomanik, et al., 2007). Self absorption and communication disturbance are inherent in the ASD phenotype (see Chapter 2, Section 2.2.1); thus, increased rates of these problems relating to increased ASD severity is, again, not unexpected. Finally, the positive association between symptom severity and behaviour problems supports previous research which has indicated raised levels of challenging behaviour in children with ASD (Totsika et al., 2011).

Lower adaptive behaviour skills were predictive of higher ADOS-G scores, a finding which aligns with reports of cognitive ability affecting Autism Diagnostic Interview-Revised (ADI-R) outcomes in children with DS (Molloy et al., 2009). The association between ASD and intellectual disability (ID) is known to be common; 40% of individuals with ID have ASD (LaMalfa et al., 2004) and around 50% of individuals with ASD have ID (CDC, 2014). Moreover, the relationship between adaptive behaviour skills (as measured by the Vineland II) and cognitive function in ASD has been shown to be mediated by the presence of low IQ (Bölte & Poustka, 2002). The findings are not unexpected, but raise concern over the validity of the ADI-R and the ADOS-G in

discriminating between profound ID and ASD in children with DS. Molloy et al. (2009), by means of an ANCOVA, showed that group differences (DS vs. DS+ASD) remained when cognitive ability was controlled for. Therefore, they concluded that increased ASD symptomatology cannot be entirely explained by more severe cognitive impairment. The latter analysis could not be replicated in the present study because the ANCOVA assumption that that the relationship between the ADOS-G domain scores and the adaptive behaviour measure (i.e. Vineland II composite) did not vary by group was violated[48]. However, the distributions of the grouped Vineland II composite scores (i.e. DS+ASD versus DS-only as determined by the ADOS-G) were inspected (see Appendix C for boxplots). As indicated by the analysis outputs, the body of DS+ASD group scores lay beneath that of the DS-only group scores. Nevertheless, the two groups were not mutually exclusive and there was an overlap in the ranges of ability. Individual case inspection revealed that two children in the DS+ASD group received a composite score of 70, one child in the DS-only group scored as low as 45, and two other children in the latter group had scores of 55. Although not supported by statistical evidence, this is an important finding as it demonstrates that autistic-type behaviour in children with DS cannot solely be explained by low levels of ability. It is not to say, however, that the level of ID in this group is not a risk factor. In fact, correlation analysis indicated that the ADOS-G total score was negatively related to the Vineland II composite score ($r=-.71$, $p<.001$).

10.4 Differences in parent and teacher reports of challenging behaviour

- Group differences (DS-only vs. DS+ASD) on *disruptive behaviour, social relating* and *anxiety* scales were found on the DBC-T but *not* the DBC-P
- Intra-class correlations indicated poor teacher-parent agreement on all DBC scales except *self-absorbed*

The poor teacher-parent agreement on the DBC is supported by weak intra-class correlations (range=.29-.50) reported in the DBC manual (Einfeld & Tonge, 2002). The intra-class correlations in the present study were stronger (range=.45-.85); however, only the *self-absorbed* scale provided 'good' agreement (Shrout & Fleiss, 1979). This finding further supports the mounting body of evidence indicating that stereotyped behaviours

[48] Variables that are known to distinguish between two groups should not be used to covary (Field, 2005).

(which form part of the *self-absorbed* scale on the DBC) are common in the DS+ASD group and implies that they are pervasive in nature.

Previous research has found that parents tend to report higher levels of externalising problems than teachers (Youngstrom, 2000). Although agreement for specific children was low between teachers and parents in the present study, teachers and parents reported similar group levels (see Figure 9.12). The differences in individual reports could be due to contextual factors (i.e. environmental differences between home and school) or due to disparity in the interpretation of items. Some variation was seen in the DBC scores (i.e. parent vs. teacher) for children with mild ID (Einfeld & Tonge, 2002); however, when plotted against the groups in the present study (see Figures 9.4 and 9.8) the variation appeared disproportionate. This implies that the factors leading to differences on the DBC-P and DBC-T do not affect the groups of children in the same way and is more suggestive of a contextual causation, rather than interpretation disparity.

However, Youngstrom (2000) proposed that parent depression and stress affected the level of disagreement. High levels of challenging behaviour have been associated with parent stress in the present study (see Chapter 12, Section 12.3.1); it may be that the relationship is bidirectional. Regression analysis implied that child challenging behaviour was predictive of elevated stress in parents (Table 12.2). However, elevated stress could also negatively affect tolerance thresholds and result in elevated ratings of challenging behaviour.

Whether contextual or interpretative, disparity in the ratings of challenging behaviours at home and school emphasises the differing needs of parents and teachers in supporting these children and thus has implications for intervention.

10.5 Individual differences among children in the DS+ASD group

The identified variability within the DS+ASD group should be recognised. Although there are clear benefits to identifying similarities within a group and establishing a behavioural phenotype, there are also some negatives. Behavioural phenotypes provide a holistic overview of syndromes and enable individuals around a child with a certain disorder (or in this case co-morbid disorders) to think beyond their expertise. An established phenotype can give insight into long-term outcomes for the child which can aid provision. However, behavioural phenotypes can lead to labelling and when negative attributes are identified stigma and scepticism are real concerns. Negative attributes within a behavioural

phenotype should be a focus for proactive intervention and *not* taken to be inevitable or applicable to all.

10.6 Limitations

With modest sample sizes it is difficult to know to what extent the findings from the group study can be generalised to all children with DS and co-morbid ASD. The study would have benefitted from the inclusion of the Autism Diagnostic Interview and the addition of an idiopathic ASD group. These issues are discussed further, along with more general limitations of the study, in Chapter 13.

10.7 Conclusions

The comparison of children with DS, with and without co-morbid ASD, demonstrated that the presence of ASD is associated with greater overall impairment in adaptive behaviour and higher levels of overall behaviour problems. Stereotyped movements appeared to be the most pervasive problem behaviour. Children with the co-morbidity were more likely to attend a special needs school; however, this did not appear to be as a direct result of their ASD symptom severity, but rather their adaptive behaviour level. As predicted, common functions of challenging behaviour displayed by the DS and co-morbid ASD group were sensory, self-stimulation and break in routine. Pain and/or discomfort were also identified by parents as possible causes of challenging behaviour. Differences were noted between parent and teacher reports of problem behaviours and individual variability was seen within the DS and co-morbid ASD group signifying that, although interventions are most definitely warranted for this group, they should be personalised where possible and context-specific.

Chapter 11: The effectiveness of screening children with Down syndrome for autism spectrum disorder

Outline:

This chapter examines the efficacy of the SCQ in ascertaining whether or not a child with DS has co-morbid ASD, as determined by ADOS-G scores. The DBC Autism Screening Algorithm (DBC-ASA) is presented as an alternative screening tool, and its efficacy assessed. Item validity for each measure and convergence between the two measures are evaluated. The relationships of the SCQ total scale, the DBC-ASA score and the ADOS calibrated severity score (CSS) with behaviour measures and hearing impairment are evaluated. The method, results and discussion are all presented in the chapter.

11.1 Introduction

The Social Communication Questionnaire (SCQ) has been the dominant screening tool used to estimate the prevalence of autism spectrum disorder (ASD) in the Down syndrome (DS) population (DiGuiseppi et al., 2010; Lowenthal et al., 2010; Magyar et al., 2012; Moss et al., 2013b). It is a widely used and recommended ASD screening measure; however, it was originally developed to identify idiopathic ASD *not* syndromic ASD and has been validated accordingly. Therefore, in order to help clinicians accurately identify ASD in genetic syndromes, such as DS, the screening tool needs to be validated for these groups. Certain features of genetic syndrome phenotypes may affect the accuracy of screening tools. For instance, Berument et al. (1999) cautioned that the SCQ may produce higher rates of false positives in individuals with a lower mental age. Thus, given that most individuals with DS have an intellectual disability (Hodapp, 1999), lower specificity rates may be seen in this group. Medical problems are commonly associated with genetic conditions (Berg et al., 2007) which, again, may impact on screening. An example prevalent in DS, and addressed in the present study, is hearing impairment (McPherson et al., 2007). Children with hearing impairments, like children with ASD, appear to struggle with interpreting others' mental states (Peterson, 2004). Commonalities such as this may result in false positive screens.

A number of screening measures need to be assessed to determine which may be most appropriate for certain genetic syndromes. This chapter evaluates the psychometric properties of the SCQ, which was adopted as a screener in the present study, but also the

Developmental Behaviour Checklist – Autism Screening Algorithm (DBC-ASA). The following research questions were considered:

1. Compared with the Autism Diagnostic Observation Schedule – Generic (ADOS-G), what are the sensitivity and specificity rates of different cut-off scores on the SCQ and DBC-ASA for children with DS?

2. Which SCQ and DBC-ASA items differentiate between the children with DS who meet the ASD threshold on the ADOS-G and those who do not?

3. Is there a significant correlation between the total scores of children with DS on the SCQ and DBC-ASA?

4. For children with DS, do the total scores on the SCQ and DBC-ASA, and severity scores on the ADOS, relate to:
    a. behavioural disturbance
    b. repetitive behaviours
    c. adaptive behaviour level?

5. Is the reported presence of a hearing impairment in children with DS associated with misclassification on the SCQ or DBC-ASA (compared with meeting the ASD threshold on the ADOS-G)?

11.2 Method

Participants

See Chapter 9, Section 9.1 for details of the children involved in the group study. Group comparisons in this chapter (DS+ASD vs. DS-only) utilised only the ADOS-G classified groups (i.e. children scoring above / below the ASD cut-off on the revised ADOS-G algorithm).

Measures

See Chapter 6, Section 6.2.4 for details on the SCQ, and Chapter 8, Section 8.5 for details on the DBC. The DBC Autism Screening Algorithm (DBC-ASA; Brereton et al., 2002) consists of 29 of the 96 items of the standard DBC. Factor analysis identified 26 of these

items as being predictive of autism group membership. A further 3 items (i.e. *'repeats words', 'arranges objects or routine in strict order'* and *'does not respond to others' feelings'*) were added as they were considered to be core autism characteristics. The internal consistency of the algorithm was .94. The recommended cut-off score of 17 produced sensitivity of .86 and specificity of .69. In the present study the parent-report DBC was utilised to assess the DBC-ASA since comparisons were made with the SCQ, which was also completed by parents.

Behavioural disturbances were measured by the DBC-P subscales (*disruptive behaviour, self-absorbed, communication disturbance, anxiety,* and *social relating*), repetitive behaviours by the Repetitive Behaviour Questionnaire (RBQ) subscales (*stereotyped behaviour, compulsive behaviour, restricted preferences, insistence on sameness,* and *repetitive speech*) and adaptive behaviour by the Vineland II composite score and subscales (*communication, daily living,* and *socialisation*) (see Chapter 8, Sections 8.4 and 8.5 for details on these measures and the ADOS-G).

Given that there was substantial item overlap between the DBC-ASA screening tool and assessment of behavioural disturbance (also measured by the DBC), it was not considered legitimate to run analyses comparing these scales. The analyses would include the comparison of the *same* responses which would, of course, indicate a relationship between the constructs and skew the overall findings making the interpretation less meaningful.

Statistical analysis

To examine the sensitivity and specificity of the screening tools, comparisons were made between being screened 'likely to have ASD' and meeting the ASD threshold on the ADOS-G. Sensitivity is the likelihood of the screening tools identifying children with DS who have ASD (according to ADOS-G scores), and was calculated using the following formula: Number of true positives / (Number of true positives + Number of false negatives). Specificity is the likelihood of the screening tools identifying children with DS who do *not* have ASD (according to ADOS-G scores), and was calculated using the following formula: Number of true negatives / (Number of true negatives + Number of false positives). The sensitivity and specificity rates are reported with 95% confidence intervals.

Participants were recruited for the group study according to the quartile division of the ordered SCQ scores from the questionnaire survey (see Chapter 8, Section 8.2 for further details). Given that the middle range of SCQ scores was specifically excluded, the

accuracy of the sensitivity and specificity rates was reduced. For this reason, they were regarded as 'approximate'. The score cut points started at the lower limit of the DS+ASD group (≥18) and a further 5 cut points were examined (i.e. up to ≥23). For the DBC-ASA (for which the full range of scores was possible), 5 cut points above and below the recommended cut point (≥17) were explored (i.e. score range=12-22).

For the item validity analysis, the number of children in each group (DS+ASD vs. DS-only) who scored positive for the autism characteristic was compared for each item using a series of chi-square tests. On both the SCQ and DBC a score of 0 indicated that the autism characteristic *was not* present, a score of 1 on the SCQ and 1 *or* 2 on the DBC indicated that the autism characteristic *was* present.

Convergence between the 2 screening tools was assessed using correlation analysis, as were relationships with behavioural disturbance, repetitive behaviour and adaptive behaviour measures. The association between the reported presence of a hearing impairment and screening misclassification was assessed using chi-square tests.

Significance level

Data were examined for significance using a <.01 p-value, and a p-value of <.05 was considered 'marginally significant' (see Chapter 8, Section 8.7, p.122 for details). Effect sizes were also reported for the chi-square tests (see Chapter 6, Section 6.2.5, p.68 for details).

Hypotheses

Based on previous research and knowledge of the ASD phenotype, it was expected that:

1. The SCQ will perform better than the DBC-ASA (in terms of sensitivity and specificity) in categorising children with DS as with/without ASD compared with the ADOS-G.
2. Total scores on the SCQ and DBC-ASA will correlate significantly and positively.
3. Scores on measures of ASD (i.e. SCQ and ADOS CSS) will correlate with scores for self-absorbed behaviour, social relating difficulties and communication disturbance on the DBC-P.
4. Scores on measures of ASD (i.e. SCQ, DBC-ASA and ADOS CSS) will correlate with scores for all repetitive behaviours measured by the RBQ.

5. The reported presence of a hearing impairment will be associated with misclassification by the screening tools.

11.3 Results

Research question 1: Compared with the ADOS-G, what are the sensitivity and specificity rates of different cut-off scores on the SCQ and DBC-ASA for children with DS?

Social Communication Questionnaire

Overall, according to outcomes on the ADOS-G, the SCQ correctly classified 36 (72.0%) of the children. Approximate sensitivity and specificity rates of various cut points on the SCQ are presented in Table 11.1.

Table 11.1 Approximate sensitivity and specificity of the SCQ when compared with ADOS-G outcomes, with corresponding SCQ cut-off scores

Score	n[a]	Approximate sensitivity	95% CI	Approximate specificity	95% CI
≥18	25	.74	.54-.87	.70	.52-.84
≥19	24	.74	.54-.87	.74	.55-.87
≥20	23	.70	.49-.84	.74	.55-.87
≥21	19	.61	.41-.78	.81	.63-.92
≥22	18	.61	.41-.78	.85	.68-.94
≥23	14	.57	.35-.76	.96	.79-1.00

[a]Number of children scoring at or above cut point

Developmental Behaviour Checklist-Autism Screening Algorithm

Application of the recommended cut-off of 17 or above resulted in 36 (72.0%) of the children being correctly classified according to outcomes on the ADOS-G[49]. Sensitivity and specificity rates of various cut points on the DBC-ASA are presented in Table 11.2.

[49] Note that although the proportions of children misclassified by the SCQ and the DBC-ASA were the same, there was some variation in the cases which were misclassified. Fourteen cases were misclassified for each measure. Ten cases were consistent across both measures. There was an association between being misclassified on the SCQ and being misclassified on the DBC-ASA (Fisher's exact, **p<.001**).

Table 11.2 Sensitivity and specificity of the DBC-ASA when compared with ADOS-G outcomes, with corresponding DBC-ASA cut-off scores

Score	n[a]	Sensitivity	95% CI	Specificity	95% CI
≥12	25	.70	.49-.84	.63	.44-.78
≥13	25	.70	.49-.84	.63	.44-.78
≥14	24	.65	.45-.81	.63	.44-.78
≥15	22	.61	.41-.78	.70	.52-.84
≥16	19	.61	.41-.78	.81	.63-.92
≥17[b]	19	.61	.41-.78	.81	.63-.92
≥18	19	.61	.41-.78	.81	.63-.92
≥19	17	.57	.37-.74	.85	.68-.94
≥20	17	.57	.37-.74	.85	.68-.94
≥21	16	.57	.37-.74	.89	.72-.96
≥22	16	.57	.37-.74	.89	.72-.96

[a]Number of children scoring at or above cut point
[b]Recommended cut point

Research question 2: Which SCQ and DBC-ASA items differentiate between the children with DS who met the ASD threshold on the ADOS-G and those who did not?

Table 11.3 shows how individual SCQ items differentiated between the children in the DS+ASD group and children in the DS-only group. Only 15 items showed statistically significant differentiation ($p<.01$). A further 8 items differentiated between the groups at a marginal level ($p<.05$). Scoring positive on 1 or more of the "best" 15 SCQ items resulted in sensitivity of .83 and specificity of .56.

The DBC-ASA items, and their differential ability (DS+ASD vs. DS-only), are listed in Table 10.4. Only 5 items showed statistically significant differentiation ($p<.01$) and a further 8 at a marginal level ($p<.05$). Scoring positive on one or more of the "best" 5 DBC-ASA items resulted in sensitivity of .87 and specificity of .41.

Table 11.3 SCQ item validity analysis

Items		χ^2	p	φ	Proportion with abnormality	
					DS+ASD	DS-only
	Communication					
2.	Conversation*	4.46	.11	.34	.40	.13
3.	Stereotyped utterances*	6.65	<.05	.41	.93	.54
4.	Inappropriate questions*	.09	.76	.05	.47	.42
5.	Pronoun reversal*	.03	.87	.03	.73	.71
6.	Neologisms*	4.78	<.05	.35	.60	.25
20.	Social chat	9.43	**<.005**	.43	.65	.22
21.	Imitation	11.92	**<.005**	.49	.52	.11
22.	Pointing to express interest	11.55	**<.005**	.48	.61	.19
23.	Gestures	6.20	<.05	.35	.57	.22
24.	Nodding to mean 'yes'	13.29	**<.001**	.52	.70	.19
25.	Head shaking to mean 'no'	6.20	<.05	.35	.57	.22
34.	Imitative social play	3.24	.20	.26	.39	.19
35.	Imaginative social play	6.80	**<.01**	.37	.74	.37
	Reciprocal Social Interaction					
9.	Inappropriate facial expressions	3.83	.05	.28	.22	.04
10.	Use of other's body to communicate	2.16	.14	.21	.65	.44
19.	Friends	6.33	<.05	.36	.65	.30
26.	Eye gaze	12.13	**<.005**	.49	.57	.11
27.	Social smiling	4.67	.10	.31	.35	.11
28.	Showing and directing attention	9.46	**<.005**	.44	.61	.19
29.	Offering to share	7.94	**<.01**	.40	.70	.30
30.	Seeking to share enjoyment	11.77	**<.005**	.49	.57	.11
31.	Offering comfort	11.55	**<.005**	.48	.61	.19
32.	Quality of social overtures	10.65	**<.01**	.46	.43	.07
33.	Range of facial expressions	10.65	**<.01**	.46	.43	.07
36.	Interest in children	7.78	**<.01**	.40	.65	.26
37.	Response to other children's approaches	3.69	.06	.27	.57	.30
39.	Imaginative play with peers	9.07	**<.005**	.43	.83	.41
40.	Group play	9.91	**<.01**	.45	.65	.26
	Restricted, Repetitive & Stereotyped Behaviour					
7.	Verbal rituals*	2.13	.35	.23	.33	.25
8.	Compulsions and rituals	6.19	.05	.35	.70	.41
11.	Unusual preoccupations	8.11	<.05	.40	.52	.19
12.	Repetitive use of objects	4.44	.11	.30	.61	.33
13.	Circumscribed interests	5.62	.06	.34	.39	.11
14.	Unusual sensory interests	2.35	.31	.22	.35	.33
15.	Hand and finger mannerisms	7.07	<.05	.38	.70	.33
16.	Complex body mannerisms	6.75	<.05	.37	.48	.15

*Verbal children only

Table 11.4 DBC-ASA item validity analysis

Items		χ^2	p	φ	Proportion with abnormality	
					DS+ASD	DS-only
2.	Avoids eye contact	3.79	.05	.28	.61	.33
3.	Aloof, in his/her own world	0.35	.56	.08	.57	.48
5.	Arranges objects or routine in a strict order	2.01	.16	.20	.61	.41
14.	Deliberately runs away	0.35	.56	.08	.57	.48
18.	Doesn't respond to others' feelings	5.06	<.05	.32	.43	.15
25.	Flicks, taps, twirls objects repeatedly	3.69	.06	.27	.57	.30
28.	Gets obsessed with an idea or activity	0.03	.87	.02	.65	.63
31.	Has temper tantrums	1.64	.20	.18	.83	.67
34.	Makes non-speech noises	6.80	**<.01**	.37	.74	.37
35.	Impatient	3.22	.07	.25	.83	.59
42.	Laughs or giggles for no obvious reason	9.63	**<.005**	.44	.57	.15
43.	Lights fires	0.87	.35	.13	.00	.04
44.	Likes to hold or play with an unusual object	6.20	<.05	.35	.57	.22
47.	Mood changes rapidly for no apparent reason	4.84	<.05	.31	.52	.22
50.	Overactive, restless, unable to sit still	1.75	.19	.19	.48	.30
53.	Overly attention seeking	1.09	.30	.15	.48	.33
55.	Poor sense of danger	4.73	<.05	.31	1.00	.81
57.	Prefers to do things on his/her own	0.73	.40	.12	.57	.44
58.	Preoccupied with only one or two interests	3.63	.06	.27	.49	.22
60.	Repeated movements	15.51	**<.001**	.56	.70	.15
61.	Resists being cuddled, touched or held	7.28	**<.01**	.38	.39	.07
63.	Repeats the same phrase or word over and over	8.31	**<.005**	.41	.48	.11
64.	Smells, tastes or licks objects	5.35	<.05	.33	.39	.11
66.	Screams a lot	1.17	.28	.15	.17	.07
68.	Stares at lights or spinning objects	4.06	<.05	.29	.35	.11
86.	Throws or breaks objects	6.23	<.05	.35	.61	.26
89.	Unrealistically happy or elated	3.22	.07	.25	.26	.07
91.	Upset over small changes in routine	3.18	.08	.25	.70	.44
94.	Wanders aimlessly	5.82	<.05	.34	.35	.07

Research question 3: Is there a significant correlation between the total scores of children with DS on the SCQ and DBC-ASA?

As predicted by Hypothesis 2, a strong positive correlation was identified between the SCQ and the DBC-ASA total scores, r=.80, **p<.001**.

Research question 4: For children with DS, do the total scores on the SCQ and DBC-ASA, and severity scores on the ADOS, relate to scores on measures of:

a. behavioural disturbances
b. repetitive behaviours
c. adaptive behaviour level?

Contrary to Hypothesis 3, the SCQ total score correlated with *every* DBC-P subscale. The ADOS CSS performed as expected, with relationships identified across the *self-absorbed* (significant), *social relating* (marginally significant) and c*ommunication disturbance* (trend level, p=.05) subscales (see Table 11.5). As predicted by Hypothesis 4, the SCQ total score and the DBC-ASA score correlated with *every* RBQ subscale, whereas the ADOS CSS only correlated with the *stereotyped behaviour* subscale (see Table 11.6). Significant correlations were seen across *all* ASD measures and *all* adaptive behaviour scales (see Table 11.7).

Table 11.5 Correlations between the DBC-P subscales and the SCQ total score / ADOS CSS

	DBC-P scales				
Measure of ASD	Disruptive Behaviour	Self-Absorbed	Comm' Disturbance	Anxiety	Social Relating
SCQ total score	**.38****	**.86*****	**.59*****	**.46****	**.69*****
ADOS CSS	.16	**.52*****	.28†	.06	**.37***

Bold indicates spearman's rho >.30, *significant at the p<.05 level, **significant at the p<.01 level, ***significant at the p<.001 level, †p=.05

Table 11.6 Correlations between the RBQ subscales and the SCQ total score / DBC-ASA / ADOS CSS

	RBQ scales				
Measure of ASD	Stereotyped behaviour	Compulsive behaviour	Restricted preferences	Insistence on sameness	Repetitive speech
SCQ total score	**.81*** **	**.48** **	**.57*** **	**.41** **	**.54** **
DBC-ASA	**.79*** **	**.49** **	**.32***	**.60*** **	**.50** **
ADOS CSS	**.49*** **	.06	.18	.12	.24

Bold indicates spearman's rho >.3, * significant at the p<.05 level, **significant at the p<.01 level, ***significant at the p<.001 level

Table 11.7 Correlations between the Vineland II composite and subscales and SCQ total score / DBC-ASA / ADOS CSS

	Vineland II scales			
Measure of ASD	Composite	Communication	Daily living	Socialisation
SCQ total score	**-.79*** **	**-.80*** **	**-.74*** **	**-.76*** **
DBC-ASA	**-.75*** **	**-.71*** **	**-.76*** **	**-.76*** **
ADOS CSS	**-.60*** **	**-.60*** **	**-.56*** **	**-.76*** **

Bold indicates spearman's rho >.3, ***significant at the p<.001 level

Research question 5: Is the reported presence of a hearing impairment in children with DS associated with misclassification on the SCQ or DBC-ASA (compared with meeting the ASD threshold on the ADOS-G)?

Overall there were 9 children who were reported as having a hearing impairment. Amongst these, 7 (77.8%) were misclassified by the SCQ. There was a significant association between the reported presence of a hearing impairment and misclassification by the SCQ (Fisher's exact, **p<.01**). Five (55.6%) of the children with a reported hearing impairment were misclassified by the DBC-ASA. The association between the reported presence of a hearing impairment and misclassification by the DBC-ASA was *not* significant (Fisher's exact, p=.09).

11.4 Discussion

Main findings

As expected, the SCQ performed better than the DBC-ASA in categorising children with DS with/without ASD[50]; the total scores on the 2 screening measures correlated significantly; the ADOS CSS correlated (at trend level and above) with self-absorbed behaviour, social relating difficulties and communication disturbance; the SCQ and DBC-ASA correlated with all repetitive behaviours; and the reported presence of a hearing impairment was associated with misclassification by the SCQ. However, contradicting Hypotheses 3, 4 and 5, the SCQ correlated with *all* behaviour scales; the ADOS CSS only correlated with stereotyped behaviours; and the reported presence of a hearing impairment was *not* associated with misclassification by the DBC-ASA.

Efficacy of screening

Comparability with previous studies of the effectiveness of the proposed SCQ cut-off for ASD (≥15) with children with DS could not be achieved in this study as the sampling strategy for the group study resulted in the exclusion of the mid-range of SCQ scores (see Chapter 7, Section 7.2). However, the SCQ score ranges utilised (DS+ASD ≥18; DS-only ≤7) resulted in an overall efficacy of 72% (proportion of children correctly classified according to ADOS-G outcomes). The upper cut-off score of ≥18 has been put forward as the most appropriate for children with DS by Lowenthal et al. (2010), with sensitivity and specificity of .77 and .93 respectively. The approximate sensitivity produced by the present study was similar at .74, although approximate specificity was lower at .70. Lowenthal et al. (2010) noted that intellectual disability affects the specificity of screening tools such as the SCQ. It may be that the disparity between the specificity rates (.93 vs. .70) can be attributed to the ability levels of the samples; however, Lowenthal et al. (2010) do not provide information on the ability of their sample. In an idiopathic ASD sample, the cut-off score of ≥18 yielded sensitivity of .83 and specificity of .85 (Witwer & Lecavalier, 2007). Inspection of Table 10.1 indicates that the cut-off score of ≥19 was the most appropriate in the present study (sensitivity=.74, specificity=.74).

Magyar et al. (2012) found that adjustment of the proposed cut-off score of ≥15 did not improve the effectiveness of the SCQ total score (if sensitivity was improved the specificity suffered greatly). Magyar et al. (2012) produced sensitivity and specificity

[50] Based on the best performing cut-off score. It must be noted that only 'approximate' sensitivity and specificity rates were determined for the SCQ given the fact that the middle range of scores was missing.

scores of .73 and .76 respectively for the recommended cut-off of ≥15 with a sample of children with DS. DiGuiseppi et al. (2010) (who also used ≥15 with children with DS) produced sensitivity and specificity scores of 1.0 and .57 respectively. The recommended SCQ cut-off score produced sensitivity .86 and specificity .78 in a sample without DS (Charman et al., 2007). Although it was not possible to assess the recommended cut-off in the present study, the aforementioned studies demonstrate that there has been some variability in the effectiveness of the cut-point. The Magyar et al. (2012) paper was used as justification for the application of the cut-off to the questionnaire survey in this project (see Chapter 6).

The DBC-ASA was considered as an alternative screening tool. Based on overall efficacy of correctly classified children the 2 measures (SCQ & DBC-ASA) were equal in their screening ability (i.e. 72% accurate). The convergence between the 2 screening tools was very good (r=.80), especially given the fact that the version of the SCQ utilised in the present study measures autism characteristics over the lifetime and the DBC only measures behaviours from the last 6 months. The recommended cut-off score for the DBC-ASA (≥17) performed relatively poorly with children with DS in terms of sensitivity compared with children with idiopathic ASD (.61 versus .94); however, specificity was much greater (.81 versus .46) (Witwer & Lecavalier, 2007). Witwer and Lecavalier (2007) argued that greater emphasis should be placed on the sensitivity of the screening tool because its purpose is to identify at-risk children, and upon passing the threshold on the screening tool a more comprehensive assessment will be advised. Following this reasoning, findings from the present study indicate that a DBC-ASA cut-off of ≥13 may be more appropriate as the sensitivity is improved to .70 but the specificity remains adequate at .63. Compared with the SCQ best outcome (cut score ≥19; sensitivity=.74, specificity=.74), the DBC-ASA was poorer at categorising the children compared with ADOS-G outcomes.

The item validity analyses indicated that, for both screening measures, some items were better than others at discriminating between the DS+ASD and DS-only groups. This suggests that shorter versions of the questionnaires may be more appropriate; not only would shorter measures perhaps yield more accurate results, they would certainly be quicker and easier to administer. Although specificity suffered, both a 15 "best" item SCQ scale and a 5 "best" item DBC-ASA scale (on which only 1 or more autism characteristic needs to be identified for the child to screen positive) resulted in good sensitivity scores that were better than the full scale sensitivity.

Whichever scale is chosen, the need for a more comprehensive assessment post-screening cannot be overstated. Although high predictive value is desirable in a screening

tool, false ASD positives, and false negatives, are likely in *any* population including children with DS. Witwer and Lecavalier (2007) championed higher sensitivity rates because false negatives may deprive children of clinical and educational resources and/or overburden parents. However, false positives can also have a negative impact. The follow-up assessments are costly and an initial 'positive' screen which is later refuted can create unnecessary parent anxiety.

Relationships with behaviour measures

Significant correlations were expected with the *self-absorbed, social relating* and *communication disturbance* subscales of the DBC-P given that these behaviours are all attributes of ASD (see Chapter 2, Section 2.2.1). *Anxiety* and *disruptive behaviour*, although common to people with ASD, do not form part of the diagnostic criteria. Screening tools for ASD should not, therefore, be biased by high rates of these latter two behaviours.

The ADOS-G calibrated severity score (CSS) performed as expected; however, both the SCQ and the DBC-ASA scores were significantly correlated with *every* behaviour scale suggesting that the efficacy of both tools is affected by disruptive and anxious behaviour. The very high correlation between the DBC-ASA and the *self-absorbed* scale (r=.92) suggests that both are measuring the same construct. As noted the 2 scales share many items; 15 of the 29 items selected for the DBC-ASA are from the *self-absorbed* scale.

All of the forms of repetitive behaviour measured by the RBQ subscales have been reported in the ASD phenotype; thus relationships with each were expected. This was the case for the SCQ and the DBC-ASA; however, the ADOS CSS only correlated with the *stereotyped behaviour* subscale. This may be a reflection on the low sensitivity of the ADOS-G to repetitive behaviours; parent reports (such as the SCQ and DBC-ASA) are able to draw upon months of observation to identify repetitive behaviours, whereas the ADOS-G is reliant on the repetitive behaviour being displayed within a 20-60 minute window. However, the RBQ in addition to the ADOS-G (as in the present study) allowed for identification of repetitive behaviours that were not displayed during the ADOS-G. Thus, the comparison of rates of repetitive behaviours (DS+ASD vs. DS-only) identified by the RBQ and based on ADOS-G groupings, as used in the present study, would appear to be valid.

Strong negative relationships were found between all of the ASD measures (SCQ / DBC-ASA / ADOS CSS) and the Vineland II adaptive behaviour subscales.

Although all of the correlations were highly significant according to p values, the ADOS CSS correlations were consistently lower than those for the screening tools (with the exception of the *socialisation* subscale which was .76 for all 3 measures). Berument et al. (1999) cautioned that the SCQ may produce higher rates of false positives in individuals with a lower mental age. False positives would affect the specificity of the screening tool. Given that most individuals with DS have ID (Hodapp, 1999), lower specificity rates should be expected in this group. Lower specificity, compared with idiopathic ASD samples, has been noted in a DS sample (DiGuiseppi et al., 2010); however, studies investigating the efficacy of the SCQ in children with DS have yielded mixed results (see p. 176-177).

The concept of 'false positives' in individuals with lower mental age needs to be considered in the context of this thesis; it could be argued that children with DS who present with autistic-type behaviour do so because of their low level of cognitive functioning. It is important to note that the present study is investigating autistic-type behaviour and that full clinical assessments were *not* conducted with the DS+ASD group. It has been demonstrated that ability is not the sole contributory factor (see Chapter 10, Section 10.3), but as outlined in the introductory chapters (see Chapter 2, Section 2.6), the Intellectual Disability (ID) associated with many genetic syndromes, including DS, may increase the risk that ASD or 'autistic-like behaviours' will be identified (Skuse, 2007).

Relationship with impaired hearing

Even with conventional hearing aids, children with hearing impairment have been shown to perform at the level of peers with ASD on theory of mind tasks (Peterson, 2004). This finding indicates that children with hearing impairment may falsely screen positive for ASD. Given that hearing impairment is common in children with DS (McPherson et al., 2007), the relationship between the presence of a hearing impairment and misclassification on the screening tools was investigated. A positive association was found with the SCQ, but not the DBC-ASA. This implies that the SCQ is more susceptible to the misclassification of hearing impaired children with DS. However, the sample of children with a hearing impairment was very small (n=9); therefore, further investigation is necessary before conclusions can be drawn.

11.5 Limitations

The accuracy of the SCQ sensitivity and specificity rates was adversely affected by the exclusion of the mid-range of SCQ scores, and only the cut points within the DS+ASD group score range were examined. However, approximate rates were produced which give insight into the applicability of the SCQ to screening children with DS for ASD. Further, more general limitations of the study are discussed in Chapter 13.

11.6 Conclusions

Both the SCQ and the DBC-ASA are adequate screening tools to use with children with DS. Given a choice of the 2, clinicians should probably opt for the SCQ as it marginally outperformed the DBC-ASA. Reduced versions of each measure may prove useful, providing good specificity and simplifying the screening process. Clinicians should be mindful of anxious and disruptive behaviour, as well as hearing impairments, when screening children with DS for ASD as these factors may affect the SCQ and DBC-ASA outcomes.

PART D: IMPACT ON THE FAMILY

Chapter 12: The impact on the family of raising a child with Down syndrome and co-morbid autism spectrum disorder

Outline:
This chapter outlines the rationale for studying the impact of raising a child with DS and co-morbid ASD on parents and siblings. The key research questions of the study are listed. The method is described, including participants, measures, statistical analyses and hypotheses. The findings are reported and discussed in the context of previous research.

12.1 Introduction

With the widely perceived 'Down syndrome advantage' (see Chapter 5), the pressures of raising a child with Down syndrome (DS) and co-morbid autism spectrum disorder (ASD) may go undetected. After all, DS is usually the primary diagnosis (often easily recognised by physical traits) and obtaining a clinical diagnosis of ASD can be difficult (Patterson, 1999). Although there is evidence that raising a child with ASD can adversely affect parents' quality of life (Mugno et al., 2007), the co-occurrence of DS and ASD may present unique challenges to parents. Siblings, too, need to be considered. Sibling relationships are an important context for social and emotional development (Whiteman et al., 2011); thus, the behavioural disturbances associated with DS and co-morbid ASD may affect the behavioural and emotional outcomes of siblings. This study aimed to answer the following research questions:

1. Are there differences between parents of children in the DS+ASD group and parents of children with DS only with respect to levels of:
    a) stress
    b) psychological morbidity
    c) perceived support?

2. Do the following factors affect the level of stress and/or the level of psychological morbidity experienced by parents:
    a) ASD severity of child with DS
    b) adaptive behaviour skills of child with DS
    c) challenging behaviour of child with DS
    d) level of perceived support?

3. Do the levels of behaviour problems differ between the siblings of children in the DS+ASD group and the siblings of children in the DS-only group?

4. Do the following factors affect the level of behaviour problems displayed by siblings:
    a) sibling age
    b) sibling gender (male vs. female *and* same gender vs. different gender siblings)
    c) ASD severity of child with DS
    d) adaptive behaviour skills of child with DS
    e) challenging behaviour of child with DS
    f) level of parent stress
    g) level of parent psychological morbidity?

12.2 Method

Section 12.2.1 Participants

The main caregiver of each child completed questionnaire measures. Information was requested on the siblings of the child with DS, if the sibling was aged between 4 and 16 years (to correspond to the age restrictions of the questionnaire utilised; see Section 12.2.3). Following the guidance of Cuskelly and Gunn (2006), siblings were only included in the analysis if they were within 4.5 years of the child with DS. A wider age gap could result in a weaker relationship between the siblings, and a restriction generates some consistency. Parents and siblings were split into 2 groups according to whether their DS child was in the DS+ASD or DS-only group according to Autism Diagnostic Observation-Generic (ADOS-G) scores. However, all main analyses were run a second time using only those participants whose ADOS-G and Social Communication Questionnaire (SCQ) scores were consistent (i.e. the "consistent" groups); any differences were reported in footnotes (see Chapter 9, Section 9.1 for further details on group classification).

Section 12.2.2 Parent measures

Questionnaire on Resources and Stress (QRS-F; Friedrich, Greenberg & Crnic, 1983)

The Questionnaire on Resources and Stress was originally developed by Holroyd (1974) to assess the negative impact of having a child with a disability. The QRS-F (Friedrich et al., 1983) is a 52 item short form that provides a total score for *stress,* as well as subscale scores for: *parent and family problems, pessimism, child characteristics,* and *physical*

incapacitation. Hastings and Johnson (2001) suggested that the child characteristics and physical incapacitation subscales exaggerated the lack of ability in children with ASD and did not directly measure parental well-being. Instead, they proposed a 31 item scale with *child characteristics* and *physical incapacitation* items omitted. Although factor analysis failed to support the use of the subscales, excellent levels of internal consistency were achieved on the total score (Kuder-Richardson coefficients ranging from .85-.93) (Honey, Hastings & McConachie, 2005), which is utilised in the present study.

General Health Questionnaire –12 items (GHQ-12; Goldberg & Williams, 1988)

The GHQ-12 is a 12 item questionnaire that screens for psychological morbidity (i.e. anxiety disorders / depression). Each item is rated on a 4-point scale. In the present study 2 scoring methods were adopted, dependent on the analysis. The presence of psychological morbidity was computed using the conventional binary method (0-0-1-1). The recommended threshold score of 3 or more was adopted (Bellantuono et al., 1987). However, when considering correlations with other measures, the classical Likert score (0-1-2-3) was adopted, which yielded a total score ranging 0-36 (Tabolli et al., 2011). When compared to the Composite International Diagnostic Interview (CIDI, World Health Organisation, 1990), the GHQ-12 was found to be a robust short form instrument (Aalto et al., 2012). It has also been shown to have excellent internal reliability (Cronbach α=.89) (Baker et al., 2009).

Interpersonal Support Evaluation List (ISEL; Cohen et al., 1985)

The ISEL is a 40 item questionnaire designed to measure perceived social support. Each item is rated on a 4-point scale (*definitely false/probably false/ probably true /definitely true*), producing a total score between 0-120; higher scores indicate a greater level of social support. The measure also produces subscales for *tangible support, belonging support, self-esteem support* and *appraisal support*. Total scale means, in the general population, range from 32.9 to 34.4 (Cohen, et al., 1985). A high level of reliability has been reported for this measure (Cronbach α=.90) (Bigatti et al., 2011).

Section 12.2.3 Sibling measure

Strengths and Difficulties Questionnaire (*SDQ;* Goodman, 1997)

The SDQ is a screening measure for the psychological adjustment of children and young people (see Chapter 6, Section 6.2.4 for description).

Section 12.2.4 Statistical analysis

See Chapter 6, Section 6.2.5 for details on how the spread of the data was assessed and how group comparison tests were selected.

Regression analyses were used to evaluate the factors contributing to parent stress, parent psychological morbidity and sibling behaviour problems. This was the preferred method of statistical analysis, instead of partial correlations, because it clarifies which variables explain the most variance and describes the direction of the correlation. The independent variables considered for the analyses were determined by previous research (see Chapter 5). The inclusion of parent measures (i.e. parent stress and parent psychological morbidity) in the sibling behaviour analysis was based on Hastings' (2002) model (see Figure 5.1). The inclusion of the adaptive behaviour of the child with DS in the sibling behaviour analysis was based on the adverse effect previously noted on parent outcomes (previous research on sibling outcomes was not available). For both analyses, in the case of challenging behaviour, the DBC-P was chosen over the DBC-T given the focus on the home setting. A variable was only included in the regression analysis if:

- It significantly correlated with the outcome variable where $r \geq .30$, $p < .01$
- In the case of dichotomous categorical independent variables (e.g. gender) there was a significant difference ($p < .01$) in the scores on the dependent variable (e.g. sibling behaviour) between the two groups of the categorical variable (e.g. male vs. female)

These criteria were employed to ensure that only variables that were likely to have any effect on the outcome variable were included in the regression analyses (the more independent variables that are included, the less power there is to detect a finding). When more than 1 variable was included, a stepwise approach was taken to extract the best subset for use in the model.

Power analyses

Although recruitment was dependent upon the numbers recruited for the group study, power analyses were conducted in order to get an indication of sufficient numbers for the analyses. The goal of the proposed study was to test the null hypothesis that the 2 population means were equal. The criterion for significance (alpha) was set at .05. The tests were 2-tailed, so an effect in either direction could be interpreted. Results from previous research into parent well-being and sibling adjustment (ASD vs. DS) were utilised so that reasonable effect sizes, which could be anticipated in the current study, were used in the power analyses. The first power analysis was based on an ASD/DS parent

group difference observed on the QRS-F *family problems* scale by Griffith et al. (2010) (see Section 12.2.2 for details on the QRS-F). The computation assumed the mean difference was 5.16 (corresponding to means of 8.64 and 3.48), the effect size was 1.56, and the common standard deviation was 3.30. With power of 95%, the proposed sample size was 12. The second power analysis was based on an ASD vs. DS sibling behaviour comparison (no group difference was identified) using the externalization scale of the Child Behaviour Checklist (CBCL; Achenbach & Edelbrock, 1983) (Rodrigue et al., 1993). The computation assumed the mean difference was 4.20 (corresponding to means of 55.95 and 51.75), the effect size was .52, and the common standard deviation was 8.16. With power of 95%, the proposed sample size was 100. A reduction in power to 80% produced a proposed sample size of 61. Given the proposed sample size of n=25 per group for the group study (see Chapter 8, Section 8.2), the analyses indicate that enough power should be achieved to identify a group difference on the parent measures; however, the sibling group comparison may be underpowered.

Missing data

For the QRS-F, ISEL and SDQ missing items were prorated at subscale level if the informant completed 75% of the relevant subscale. For the GHQ-12 missing data resulted in the participant being excluded from analyses.

Significance level

Data were examined for significance using a <.05 p-value. As several hypothesised factors were put forward for the regression analyses, to reduce the chance of obtaining type I errors (i.e. false positive results), statistical significance for the correlation analyses (and pair wise tests for categorical independent variables) was determined by a p-value of <.01. Effect sizes were also reported (see Chapter 6, Section 6.2.5, p.68 for details).

Section 12.2.5 Hypotheses

Based on previous research findings, several hypotheses were made about: (1) parent group comparisons, (2) factors affecting levels of parental stress and psychological morbidity, (3) sibling group comparisons, (4) factors affecting levels of sibling behaviour problems.

1. Compared with parents of children with DS only, parents of children in the DS+ASD group will:
   a) report experiencing more stress on the QRS-F
   b) be more likely to report psychological morbidity at a clinical level on the GHQ-12
   c) report less support on the ISEL

2. Parents will be more likely to report experiencing high levels of stress and psychological morbidity if:
   a) their child with DS has more severe ASD symptoms (as measured by the ADOS CSS)
   b) their child with DS has low adaptive behaviour skills (as measured by the Vineland II)
   c) their child with DS shows high levels of challenging behaviour (on the DBC-P)
   d) they perceive a low level of support (as measured by the ISEL)

3. No differences will be identified in the levels of behaviour problems reported for siblings of children in the DS+ASD group and siblings of children in the DS-only group.

4. Siblings will be more likely to display general behaviour problems (as measured by the SDQ) if:
   a) they are young
   b) they are female (specifically 'conduct' problems)
   c) they are the same gender as their DS sibling
   d) their DS sibling has more severe ASD symptoms (as measured by the ADOS CSS)
   e) their DS sibling has low adaptive behaviour skills (as measured by the Vineland II)
   f) their DS sibling shows high levels of behaviour problems (on the DBC-P)
   g) their parent reports a high level of stress (on the QRS-F)
   h) their parent reports a high level psychological morbidity (on the GHQ-12)

12.3 Results

Section 12.3.1 Parent well-being

Of the parents (n=50), 44 (88.0%) mothers and 6 (12.0%) fathers completed the questionnaire measures.

Research question 1: Are there differences between parents of children in the DS+ASD group and parents of children with DS only with respect to levels of:

a.) stress

b.) psychological morbidity

c.) perceived support?

As predicted parents of children in the DS+ASD group reported a significantly higher level of stress on the QRS-F31 than parents of children with DS only (t(48)=-4.02, **p<.001**, r=.50)[51] (Figure 12.1). However, contrary to predictions, there was no difference in the proportions of parents scoring above clinical cut-off on the GHQ-12 (DS+ASD=40.9%; DS-only=37%; $\chi^2(1, N=49) = .08$, p=.78, φ=.04)[52] or in levels of perceived support, as measured by the ISEL[53]. (See Figure 12.2 for group mean scores).

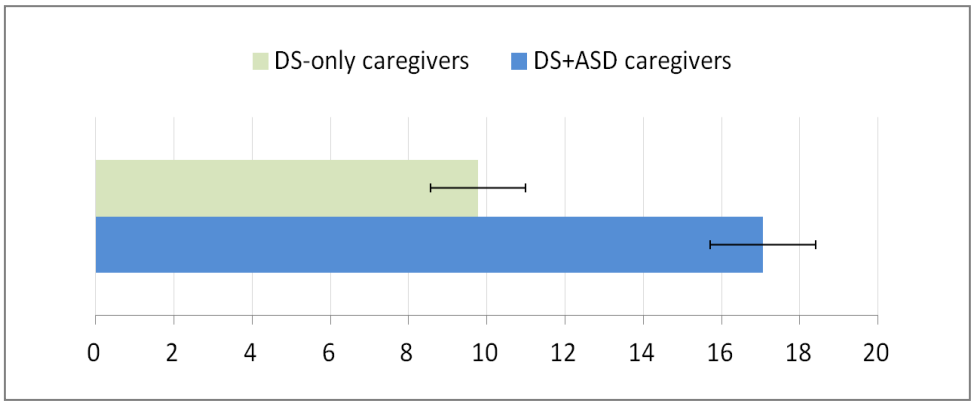

Figure 12.1 Mean parent scores on the QRS-F31 (DS+ASD vs. DS-only)

Error bars represent standard error of the mean

[51] The group difference remained with the "consistent" groups (i.e. SCQ+ADOS ratings in agreement)
[52] Missing data for 1 parent. No group difference was identified between the "consistent" groups.
[53] Comparison of the "consistent" groups resulted in a significant difference in *belonging support* (z=-2.23, **p<.05**, Cliff's d=.44), with the DS+ASD group reporting less support.

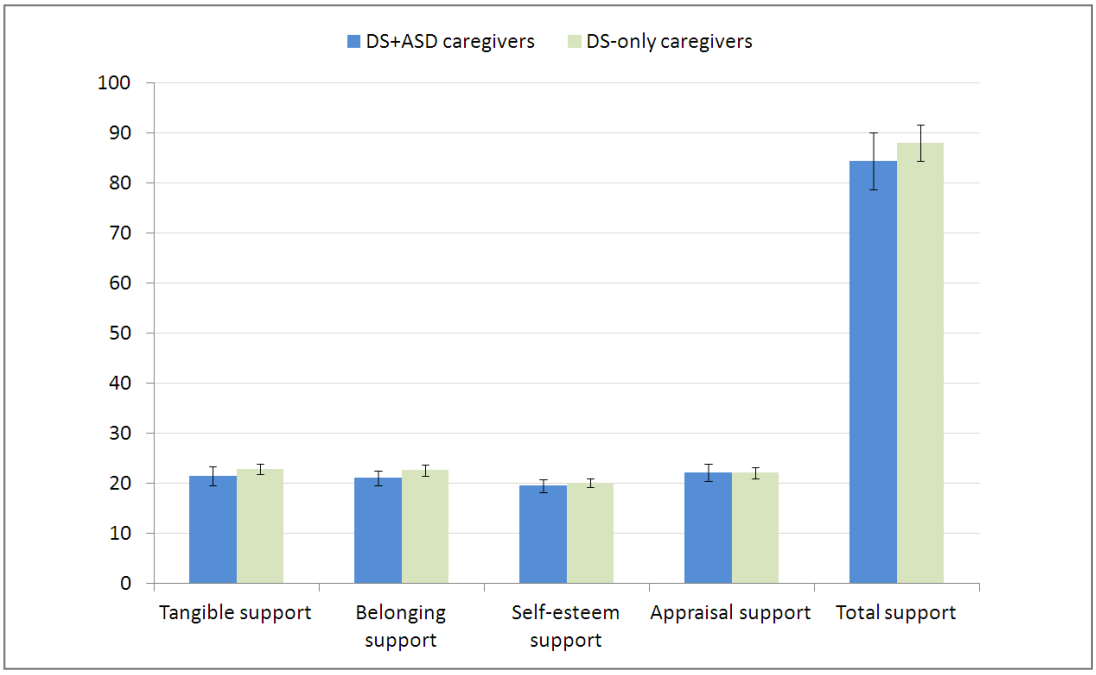

Figure 12.2 Mean parent scores on the ISEL (DS+ASD vs. DS-only)

Error bars represent standard error of the mean

Research question 2: Do the following factors affect the level of stress and/or the level of psychological morbidity experienced by parents:

a) ASD severity of child with DS
b) adaptive behaviour skills of child with DS
c) challenging behaviour of child with DS
d) level of perceived support?

As predicted, *all* of the contributory factors were related to parental stress and / or psychological morbidity (see Table 12.1). However, stepwise regression analyses identified challenging behaviour and the amount of perceived support as the main contributory factors affecting stress (see Table 12.2) and perceived support was the sole contributory factor for psychological morbidity (see Table 12.3).

The challenging behaviour of the child accounted for 57% of variance in parental stress. The amount of perceived support accounted for a further 6% (Table 12.2). The addition of perceived support improved the model ($p<.05$). Perceived support accounted for 18% of the variation in parental psychological morbidity (Table 12.3).

Table 12.1 Correlations between parent stress and psychological morbidity and hypothesised contributory factors

Factors	**Stress** (i.e. QRS-F31 total)	**Psychological morbidity** (i.e. GHQ-12 scale total)
ASD severity of DS child (i.e. ADOS CSS)	**.44****	.18
Adaptive behaviour of DS child (i.e. Vineland II composite)	**-.68*****	**-.30***
Challenging behaviour of DS child (i.e. DBC-P total)	**.72*****	**.31***
Perceived support (i.e. ISEL total)	**-.53*****	**-.46****

Bold indicates spearman's rho >.30, *significant at the p<.05 level, **significant at the p<.01 level, ***significant at the p<.001 level

Table 12.2 Variance in parent stress explained by challenging behaviour of child with DS and amount of perceived support

		β	**p**	**R^2**	**SE of estimate**
1	Challenging behaviour of DS child (i.e. DBC-P total)	.64	<.001	.57	4.96
2	Perceived support (i.e. ISEL total)	-.27	<.05	.63	4.66

Table 12.3 Variance in parent psychological morbidity explained by amount of perceived support

		β	**p**	**R^2**	**SE of estimate**
1	Perceived support (i.e. ISEL total)	-.43	<.01	.18	5.76

Section 12.3.2 Sibling behaviour

Questionnaires were completed for 44 siblings in total but 2 were excluded because the date of birth was missing and 7 were excluded because the age difference with the DS sibling exceeded 4.5 years (see Section 12.2.1). In total, data for 35 siblings were analysed (16 DS+ASD siblings; 19 DS-only siblings). (See Table 12.4 for group characteristics).

Table 12.4 Age and gender for the sibling subsamples (DS+ASD vs. DS-only)

		DS+ASD siblings	DS-only siblings	Group difference
N		16	19	
Age in years	Mean (SD) Range	12.31 (3.26) 5-16yrs	11.21 (3.65) 5-16yrs	t(33)=-.93, p=.36, r=.16
Gender	% Male (N)	62.5 (10)	42.1 (8)	χ^2 =1.45, p=.23, φ=.20

Research question 3: Do the levels of behaviour problems differ between the siblings of children in the DS+ASD group and the siblings of children in the DS-only group?

As predicted by Hypothesis 3, no group differences were identified in sibling behaviour as assessed by the SDQ[54] (see Figure 12.3 for group mean scores).

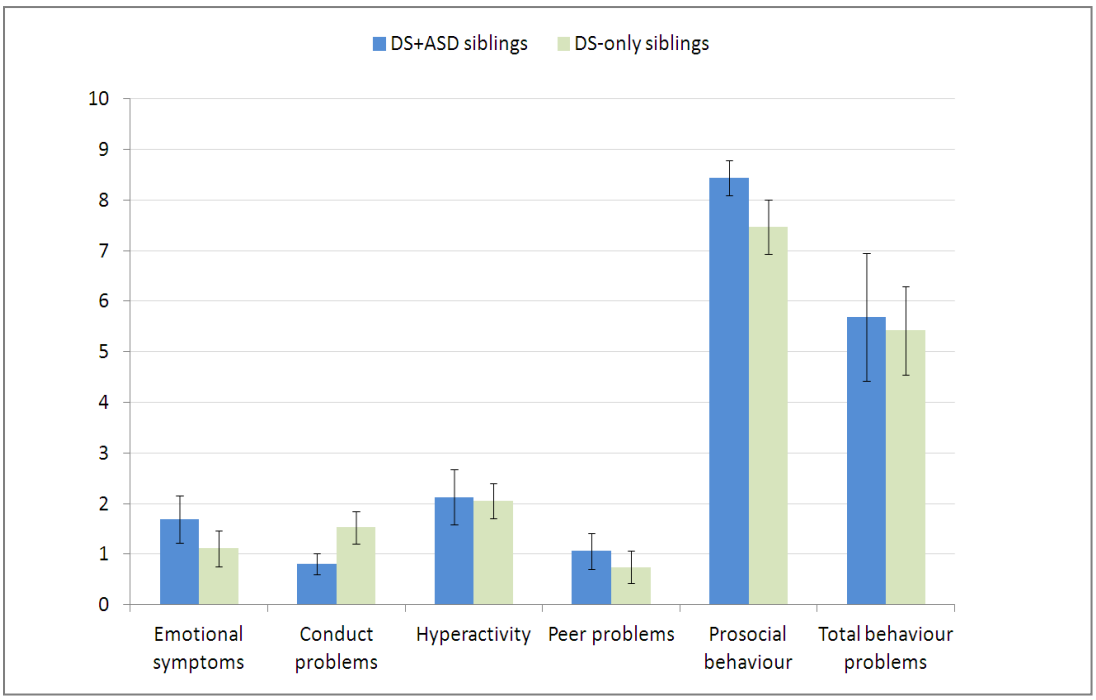

Figure 12.3 Mean sibling scores on the SDQ (DS+ASD vs. DS-only)

Error bars represent standard error of the mean

[54] This remained the case with the "consistent" groups

Research question 4: Do the following factors affect the level of behaviour problems displayed by siblings:

a) sibling age
b) sibling gender (male vs. female *and* same gender vs. different gender siblings)
c) ASD severity of child with DS
d) adaptive behaviour skills of child with DS
e) challenging behaviour of child with DS
f) level of parent stress
g) level of parent psychological morbidity?

Although Hypothesis 4.b. (that female siblings would reportedly display higher levels of conduct problems) was *not* supported, female siblings (median=1, inter-quartile range (IQR) =1-3) were reported as experiencing higher levels of emotional symptoms than male siblings (median=0, IQR=0-1), z=-2.60, **p<.01**, Cliff's d=.49. No other gender differences, including same gender *versus* different gender differences, were found (refuting Hypothesis 4.c.). Gender accounted for 19% of variance in sibling emotional symptoms (see Table 12.5).

Of the other variables hypothesised to be related to disturbance in siblings, *none* were significantly associated with overall level of behaviour problems. Nonetheless, apart from ASD severity, each of the variables was correlated with difficulties related to peer relationships (see Table 12.6). However, the association with parent stress was the only one strong enough to be included a regression analysis (see Section 12.2.4 for criteria). Parent stress accounted for 20% of variance in sibling peer problems (see Table 12.7).

Table 12.5 Variance in sibling emotional symptoms explained by sibling gender

		β	**p**	**R^2**	**SE of estimate**
1	Sibling gender	-.43	<.01	.19	1.55

Table 12.6 Correlations between sibling behaviour and hypothesised contributory factors

Factors	Emotional symptoms	Conduct problems	Hyper'	Peer problems	Total behaviour problems
Sibling age (in years)	.07	-.16	-.13	**.35***	.04
ASD severity of child (i.e. ADOS CSS)	-.08	-.20	-.06	.06	-.09
Adaptive behaviour of child (i.e. Vineland II composite)	-.29	.15	.03	**-.39***	-.11
Challenging behaviour of child (i.e. DBC-P total)	.09	-.10	-.01	**.34***	.08
Parent stress (i.e. QRS-F31 total)	.13	-.11	-.04	**.50****	.09
Parent psychological morbidity (i.e. GHQ-12 scale total)	.23	-.01	.12	**.41***	.25

Bold indicates spearman's rho >.30, *significant at the p<.05 level, **significant at the p<.01 level, ***significant at the p<.001 level

Table 12.7 Variance in sibling peer problems explained by parent stress

		β	p	R^2	SE of estimate
1	Parent stress (i.e. QRS-F31 total)	.44	<.01	.20	1.28

12.4 Discussion

Main findings

As predicted, parents of children in the DS+ASD group reported a higher level of stress than parents of children in the DS-only group. However, no group differences were identified in psychological morbidity or perceived support, except for the "consistent" DS+ASD group reporting a lower level of belonging support. Of the predicted factors only child challenging behaviour and perceived support contributed to parent stress, with perceived support also affecting parent psychological morbidity. No DS+ASD versus DS-only group differences were identified for sibling behaviour. However, female siblings were reported to show more emotional symptoms and parent stress contributed to sibling peer problems.

Parent well-being

The higher level of stress reported in the DS+ASD parent group is not surprising given that parents of children with ASD tend to report greater stress than parents of children with other developmental disabilities (Eisenhower et al., 2005). The identification of challenging behaviour as a contributory factor to raised stress levels also replicates previous findings (Esbensen & Seltzer, 2011). As the DS+ASD group were reported to show levels of behaviour problems that are similar to those found in idiopathic ASD (see Chapter 6), greater levels of stress would also be expected among their parents than in parents of children with DS only.

The "consistent" groups' outcomes on the ISEL perhaps indicate that those parents who are aware of their child's ASD symptomatology feel less 'belonging support'. The subscale focuses on meeting with people, talking to people, doing activities with others and shared interests. This indicates a need for a specific DS and co-morbid ASD support group, where parents could meet and share experiences. The contribution of perceived support to the stress *and* psychological morbidity levels of parents (albeit only accounting for a small amount of variance in each case) further supports the need to implement a specific support network for these parents (in addition to the Down's Syndrome Association which all participants were active members of at the time of initial recruitment).

Sibling behaviour

The lack of a group difference (DS+ASD siblings vs. DS-only siblings) is consistent with previous research which identified no behaviour differences between the siblings of children with idiopathic ASD and the siblings of children with DS (Rodrigue et al., 1993). However, the research finding of an increased level of conduct problems in girls who have a sibling with DS (Cuskelly & Gunn, 1993) was *not* replicated. Instead, female siblings were reportedly more likely to show emotional symptoms.

Siblings' peer relations also appeared to be adversely affected by parent stress. Hastings (2002) suggested that child behaviour and parent stress can form a negative cycle; challenging behaviour can contribute to parental stress, which affects parent behaviour, which in turn affects child behaviour (see Chapter 5, Figure 5.1). This study indicates that challenging behaviour exhibited by a child with DS can contribute to parental stress and that parental stress contributes to sibling peer problems, thus partially supporting the notion of Hastings' model.

12.5 Limitations

There are a number of limitations associated with the family impact study that restrict the conclusions that can be drawn. Although most of the respondents in the study were mothers, some fathers were also involved (and data were pooled for both mothers and fathers). Parental gender may have affected the outcomes as previous research has indicated that women report higher levels of stress, experience more psychological distress, and are more likely to attribute problems to family-related events than men (Matud, 2004). Gender stratification of the sample would have provided an interesting comparison; however, the number of fathers was too low to make this statistically viable. Moreover, the intention of the study was to assess the impact on the main caregiver regardless of gender.

In addition, the sample sizes were modest, the number of measures was limited and the measures utilised were solely informant-based. These issues are discussed further, along with more general limitations of the study, in Chapter 13, Section 13.2.

12.6 Conclusions

Parents of children with DS and co-morbid ASD report higher levels of stress than parents of children with DS only, and parent stress appears to have an adverse effect on the peer relationships of siblings. Therefore, interventions to reduce stress should be considered for this parent group. The challenging behaviour of the child with DS seems to be a contributory factor; thus, behavioural interventions may go some way in alleviating parent stress. A lack of perceived support also appears to contribute to raised stress (and psychological morbidity), and so a specific support network in addition to the Down's Syndrome Association may be welcomed.

PART E: GENERAL DISCUSSION

Chapter 13: General discussion

Outline:

This chapter covers 4 main areas:

(i) Summary of the main findings

(ii) Evaluation of the strengths and limitations of the research

(iii) Consideration of the implications of the findings

(iv) Proposals for possible avenues for future research

13.1 Summary of main findings

Section 13.1.1 Main findings from the questionnaire survey (Chapter 6)

- Over a third of children with Down syndrome (DS) in England and Wales aged 6-15 screened positive for autism spectrum disorder (ASD)
- The gender ratio of screen positive children was 2:1 male to female
- The screen positive children:
    - Showed greater levels of emotional symptoms, conduct problems and hyperactivity than children with DS who scored well below threshold on the autism screening questionnaire
    - Had poorer communication skills than the children with DS scoring well below threshold
    - More commonly demonstrated a regression in skills than the children with DS scoring well below threshold

Section 13.1.2 Main findings from the idiopathic ASD comparison study (Chapter 7)

- The screen positive children:
    - Showed an atypical autism profile (compared with individuals with idiopathic ASD)
        - They were less likely to be impaired in certain communication skills such as imitation, and in certain social interaction skills such as eye gaze, but more likely to demonstrate compulsions and rituals
    - Levels of conduct problems and hyperactivity were as high as those of an idiopathic ASD group

Section 13.1.3 Main findings from the group study (Chapters 8, 9 & 10)

- Compared with children with DS only, children in the DS+ASD group (i.e. scoring above threshold on the Autism Diagnostic Observation Schedule-Generic (ADOS-G)):
    - Had poorer adaptive behaviour skills
        - Across communication, daily living *and* socialisation domains
    - Were more likely to demonstrate most ASD characteristics during the ADOS-G, but not echolalia, stereotyped phrases, self injury or anxiety.
    - As reported by parents:
        - Demonstrated higher levels of self absorbed behaviour, self injury, physical aggression and stereotyped behaviour
        - Were more likely to demonstrate challenging behaviours due to self-stimulation, pain/discomfort, sensory reasons or because there had been a break in routine
    - As reported by teachers:
        - Demonstrated higher levels of disruptive behaviour, self-absorbed behaviour, communication disturbance and anxiety
    - As observed at school:
        - Demonstrated higher levels of stereotyped behaviour
            - Engaged in stereotyped behaviour for longer during unstructured 'play' sessions
- Individual differences were noted in the DS+ASD group

Section 13.1.4 Main findings from the screening tools study (Chapter 11)

- Both the Social Communication Questionnaire (SCQ) and the Developmental Behaviour Checklist-Autism Screening Algorithm (DBC-ASA) were identified as adequate screening tools for children with DS

Section 13.1.5 Main findings from the family impact study (Chapter 12)

- Parents of children in the DS+ASD group reported a higher level of stress than parents of children with DS only
- The challenging behaviour of the child with DS and the level of perceived support both contributed to parent stress
- The level of perceived support contributed to parent psychological morbidity
- Sibling gender affected the level of sibling emotional symptoms
- Parent stress contributed to sibling peer problems

13.2 Limitations of present research

Section 13.2.1 Sampling strategy

Representativeness of sample

The children and families involved in the research study were recruited through the Down's Syndrome Association (DSA). As there is no central register for DS in the UK, the DSA was considered the best recruitment path. It allowed for a large sample to be obtained, but the representativeness of the DSA was a concern. An estimation based on population and prevalence statistics determined that the DSA represented around a third of families with a child with DS in the age range of the study (see Chapter 6, Section 6.2.1, p.64 for estimation calculation). However, only around a third of the families contacted responded to the survey and there was no way of comparing the demographics of responders and non-responders. Despite this, the gender and genetic mechanism proportions of the sample were as expected based on knowledge of DS, and the socioeconomic status of the sample was evenly distributed.

Grouping strategy for the questionnaire survey

The formation of the DS+ASD and DS-only groups for comparative analysis with the survey data was based solely on the SCQ. The SCQ has been identified as an adequate tool in differentiating between cases of ASD and non-ASD in children with DS (Magyar et al., 2012) and a previous study has utilised the questionnaire for the formation of groups (Moss et al., 2013b). However, it must be noted that the SCQ is *not* a diagnostic tool and its imperfect screening ability may have lead to a number of type I errors (i.e. false positives) in the DS+ASD group and type II errors (i.e. false negatives) in the DS-only group.

Recruitment strategy

The questionnaire survey of England and Wales and the group study were carried out consecutively and recruitment into the group study was reliant on the outcome of the survey (see Chapter 8, Section 8.2 for more details on the sampling strategy for the group study). This resulted in a restricted number of families being eligible for the group study and although *all* of the potential families for the DS+ASD group (who had given consent) were contacted, the response rate only yielded a group size of 25. The gap in time between the survey study (when the SCQ data were collected) and the group study may also have affected the comparison between the SCQ and other measures.

Group and family impact sample sizes

Sample sizes for both the group comparison and family impact studies were reliant on previous recruitment into the survey study. However, although sample sizes were fairly modest in relation to some previous studies of this kind (e.g. Capone et al., 2005; Carter et al., 2007; Ji et al., 2011), the group study and parent sample sizes satisfied the power analyses and produced group differences with good effect sizes. The sibling sample size on the other hand was relatively small and, as a result, there is concern that the analyses may have been underpowered.

The group (i.e. DS+ASD and DS-only) sample sizes suffered for the natural observation at school because some children were visited at home (n=4) and consent was not granted for others (n=4). It was possible to observe the children at home and to include them in the analyses; however, it was thought that the inconsistency in environment may have adversely affected the validity of the study. The discrepancy in the behavioural reports of parents and teachers (see Chapter 9, Section 9.5) goes some way in supporting this possibility. The sample sizes were particularly diminished for the analysis of the percentage of time the children engaged in challenging behaviours (see Table 9.9) because only those children who had displayed the behaviours were included. However, this is an established method that has been previously conducted with similar numbers of children (Oliver et al., 2009).

Other than the natural observation, the benefit of improved sample sizes would have applied to the regression analyses. The sample sizes of the present study were deemed adequate based on examples of studies with similar samples and design (Hastings, 2003; Meltzer, 2011). There is no consensus on the approach to compute the power and sample size for regression. However, larger sample sizes would have made these statistical tests more robust.

Lack of idiopathic ASD group

Collaboration with the PLASN-R project allowed for comparison with an ASD-only sample for the questionnaire survey data. However, it would have been valuable to have an ASD-only group involved in the group study. The comparison of children with DS and co-morbid ASD with children who have DS only is greatly warranted given that the recognition and diagnosis of the co-morbidity requires the differences between these 2 groups to be elucidated. However, the inclusion of an ASD-only group would have gone some way in clarifying the distinct autism profile that was noted in the findings of the questionnaire survey.

Section 13.2.2 Outcome measures

Limited number of measures

The study would have benefitted from the addition of the Autism Diagnostic Interview-Revised (ADI-R). Unlike the ADOS-G, which allows for the observation of social communication skills, the ADI-R provides information on the child's full developmental history. In many research studies, both are central to ascertaining whether or not a child has ASD; however, the ADI-R was omitted from the present study because the children were visited at school where possible (rather than at home) and the addition of a detailed parent interview, which can take up to 3 hours to complete, was not feasible. It must also be noted that clinical expertise and judgement is also required to endorse a diagnosis of ASD and in the present study the ADOS-G assessor was *not* clinically trained. Nevertheless, the ADOS-G is a useful tool, which can be used in research for the assessment of ASD characteristics (rather than for clinical diagnosis) and good reliability rates were achieved in the present study.

The inclusion of an IQ measure may have also improved the study. Since the intellectual functioning of children with DS and co-morbid ASD has been shown to be very low (Molloy et al., 2009) and the IQ of children with DS can be rather variable (Hodapp, 1999), obtaining formal IQ data on all children would have required a number of different measures and this would have affected comparability across the groups. Instead, the Vineland II was used as a proxy measure of the general ability of the children. Although the Vineland II scores are *not* directly comparable to IQ, significant positive relationships have been found between IQ and Vineland II domain scores for low-functioning ASD and low IQ groups (Liss et al., 2011) and Perry et al. (2009) reported convergence between IQ and Vineland II composite scores for individuals with mild intellectual disability.

The inclusion of an IQ measure is particularly relevant given that the association between ID and ASD could be offered as justification for the presence of autistic-type behaviours in DS. Replication of the analysis Molloy et al. (2009) conducted with a sample of infants with Trisomy 21 and co-morbid ASD would have provided more clarity on this association in older children with DS.

Further expansion of the study design would have been warranted in the evaluation of the function of challenging behaviour. However, because of time constraints and the need to avoid overburdening parents, the Questions about Behavioural Function-Modified (QABF-M) was only administered for the behaviour that parents found "most challenging". Assessment of the function of each challenging behaviour that the child

demonstrated would have increased understanding of the meaning and utility of the behaviours. The family impact study, too, may have benefitted from the addition of family background measures. Parental age, income, marital status and autistic traits have all been considered in previous studies of this kind (see Chapter 5), but again it was not possible to collect all these data within the constraints of the study.

Pre-exposure to ASD measures

It was known that some children involved in the study had been through the ASD diagnostic process, but data on how diagnoses were obtained were not collected. It is possible, therefore, that some parents may have previously completed the SCQ, or at least been made more aware of the characteristics typical of ASD, which may have affected their ratings. Some children may have also been assessed by the ADOS-G. On some tasks the supposed novelty of the assessors' actions, for instance blowing bubbles to gauge the child's reaction, may have been affected. On others, practice effects may have occurred. For example, on the 'telling a story from a book' task (designed to obtain a sample of spontaneous language and assess understanding of emotions), prior exposure might have led the child to perform to a higher standard. However, on the rare occasions when a child indicated that they knew the book, the assessor elected to use the second book made available in the ADOS-G kit.

Section 13.2.3 Reliability of observational measures

Although observational measures have the great benefit of ecological validity, reliance on individual judgements can adversely affect reliability. Therefore, as in the case of the present study, reliability needs to be assessed by an additional rater. It is beneficial to employ 2 (or more) additional raters to assess not only the agreement with the lead rater, but to assess agreement between the additional raters. However, due to pressures of time and availability of other researchers, this was not possible. Both ADOS-G raters in the present study were officially trained (see Appendix D for the course attendance certificate of the lead rater), and both regularly attended ADOS-G coding consensus meetings.

ADOS-G reliability

Although all ADOS-G domains produced 'good' or 'excellent' inter-rater reliability (Fleiss, 1981), the level of agreement for the *restricted and repetitive behaviours* was somewhat lower (see Chapter 8, Section 8.7, p.124). This is similar to reliability rates published in the ADOS manual (live-video intra-class correlations: *social*

communication=.91, *restricted repetitive behaviour*s=.72)[55] (Lord et al., 1999). According to the ADOS manual, agreement suffers for the *restricted and repetitive behaviours* domain when live codes are compared with video codes, whereas the other domains remain unaffected. There are practical explanations for this; the camcorder may be set up in a position which restricts the view of the video rater; alternatively, the assessor may be turned away from the participant when a behaviour occurs but the camcorder has captured the behaviour.

There was also bias identified in the ratings of the second rater (ES) compared with those of the first rater (GW) (which are utilised in the analyses). The latter's ratings were more conservative in nature (scores equated to an algorithm value of 1 rather than 2), but these were considered appropriate to use as there is some contention in the literature about the classification of ASD in genetic syndromes (see Hall et al., 2010) and a more conservative approach to the detection of ASD characteristics goes some way towards preventing the mislabelling of the behaviours demonstrated by this group of children.

Natural observation reliability

Although all challenging behaviours were operationally defined, there was some concern over the interpretation of behaviours. Refusal to comply was a particular concern given that care was needed to include only those examples where the child clearly understood the request. Nevertheless, an 'excellent' rate of agreement was achieved (.93; interpretation based on Fleiss (1981)). In fact, all behaviours coded during the natural observation produced 'good' or 'excellent' inter-rater reliability (Fleiss, 1981), and an agreement range (i.e. .67-.93) similar to previous studies of this kind (see Oliver et al. (2009) for an example).

13.3 Strengths of present research

Questionnaire survey sample size

The questionnaire survey assessing the proportion of children with DS who screen positive for ASD symptoms was the largest of its kind. It was also the first to be carried out over such an extensive geographical area. The response rate exceeded that of previous studies (DiGuiseppi et al., 2010; Moss et al., 2013b). The online accessibility of the questionnaire measures for those DSA members who had email addresses may have helped to achieve the relatively good level of response.

[55] Note that intra-class correlations from the ADOS manual are based on original algorithms

Utilisation of observation measures

The present study utilised observational measures (i.e. ADOS-G for autism characteristics and a natural observation for challenging behaviours) in addition to informant-based measures. Many previous studies in this field have relied solely on informant-based measures (Capone et al., 2005; Carter et al., 2007; Castillo et al., 2008; Dressler et al., 2011; Magyar et al., 2012; Moss et al., 2013b). This is understandable given the practicality of these measures, especially with large samples. However, informant-based measures are susceptible to misinterpretation and response biases. Observations allow for an ecologically valid assessment of behaviours, although a weakness is the limited time period in which the observation takes place and whether or not a true picture will be captured in this time. Thus, the combination of informant-based measures and observations, as in the present study, maximises the advantages of both forms of data collection.

Consideration of the school context

Previous studies in this field have focussed primarily on challenging behaviours from the perspective of the parent. This is clearly crucial but, given that children in the age range of the current study spend around 30 hours a week at school during term time, information on behaviours at school is also important. Challenging behaviours in the school environment are disruptive not only to the child involved but to the other children in the class; moreover, the stress of dealing with such behaviours is a concern for teachers (Kelly et al., 2007). Identification of the challenging behaviours displayed by children with DS and co-morbid ASD at school can help to provide focus for school-based interventions.

Consideration of the impact on the family

To date, there has been little consideration of the impact of raising a child with DS and co-morbid ASD on the family. Investigation of stress levels and potential stressors was considered particularly pertinent for the present study as the strains encountered by parents of children with DS and co-morbid ASD may go undetected given the notion of the "Down syndrome advantage" (Esbensen & Seltzer, 2011) in relation to parent stress. The support network and resources that are in place for the parents of children with DS may not be directly applicable to those whose children also present with ASD characteristics.

Sibling adjustment was also considered important to measure because sibling relationships are a central context for social and emotional development (Whiteman et al.,

2011). There is some indication that siblings of children with developmental disorders, such as ASD, show raised levels of emotional and behavioural problems (Bägenholm & Gillberg, 1991; Rodrigue et al., 1993) and knowledge about sibling adjustment has implications for intervention.

13.4 Implications of findings

Improved clinical awareness and knowledge

The high number of children with DS passing the screening threshold for ASD should raise awareness of the potentially high risk of co-morbidity between the two conditions. It has been noted that making the dual diagnosis is difficult and, if achieved, tends to come late in childhood, often during adolescence (Rasmussen et al., 2001). Increased awareness of the possible association between DS and ASD should lead to improved access to clinical assessments, while better understanding of the somewhat atypical presentation of ASD symptoms in this group may aid clinicians in the diagnostic process. To give a specific example, general practitioners should not take the presence of eye contact and social smiling as a deterrent to referring a child for further assessment if the parent is reporting other characteristics typical of ASD. The child may not show obvious impairment in these social interaction skills but may still demonstrate a number of ASD characteristics that warrant a diagnosis.

A further message that clinicians can take from the research is that autism screening tools widely used in the general population (specifically the SCQ and DBC-ASA) *can* be utilised with children with DS and recommended cut-off scores are applicable. However, care should be taken when interpreting these scores and, although caution is applicable across all groups (as screening tools should *not* be viewed as diagnostic tools), the present research highlighted that particular care should be taken when screening children with DS who have a hearing impairment. The clinical assessment should also monitor levels of disruptive or anxious behaviour, as these may inflate scores on the autism screening instruments.

With due care and attention to the particular problems of diagnosis in this group, there are potentially great benefits to the family in obtaining a clinical diagnosis. For instance, an ASD diagnosis may help attain a more appropriate school placement (see Chapter 6, Section 6.6.8 for further details), and help parents to better understand why their child with DS is so different from the characteristic stereotype.

Search for genetic markers of ASD

Detailed information about ASD in genetic syndromes, such as DS, is potentially important for ASD genetic research. For instance, the atypicalities in presentation compared with idiopathic ASD could be linked to the associated genes (chromosome 21 in the case of DS; see Chapter 1, Section 1.4). A 'buffer' effect of the presence of DS is possible when considering the relative strength in reciprocal social communication skills identified by the analysis of SCQ items (see Chapter 7). The less pronounced gender ratio seen in DS and co-morbid ASD, as compared with idiopathic ASD, is also of interest. It could be that DS in some way protects males from the risk of ASD, or it could amplify the risk in females.

Sakai et al. (2011) used genes associated with ASD to develop a protein interaction network. Most of the identified genes (and related proteins) were linked to syndromic ASDs; however, converging pathways were considered to give insight into idiopathic ASD. Convergence was identified around some proteins, but only one overlapping gene on chromosome 21 was identified in the network. This finding is suggestive of atypicalities in DS and co-morbid ASD compared with other ASD presentations.

Behavioural intervention

The corroboration of poor adaptive behaviour skills in this group of children, including relative deficits in communication, daily living *and* socialisation skills compared with children with DS only, supports the need for interventions. Early interventions have been shown to be effective in improving adaptive behaviour (Reichow, 2012), language (Magiati, Tay & Howlin, 2012), and social communication (Kasari & Patterson, 2012) skills in children with ASD and thus may also be appropriate for children with DS and co-morbid ASD.

The reports of high levels of challenging behaviours in this group also indicate the need for interventions for problem behaviours. Brosan and Healy (2011) have identified a number of behaviourally-based interventions that are effective in reducing aggression in children with developmental disabilities. The functions of challenging behaviour identified in the present study (see Chapter 10, Section 10.2.2, p.159) may help to advise parents of children with DS and co-morbid ASD of suitable interventions. Moreover, the differing challenges reportedly faced by parents and teachers may help to determine the focus of intervention in each setting (i.e. home and school).

Parent intervention

The identification of a higher level of reported stress in the DS+ASD parent group (compared with parents of children with DS only) indicates the need to provide support for these families. Previous research has indicated that equipping parents with the skills to manage their child's behaviour through training in behavioural principles can lead to reduced stress (Feldman & Werner, 2002). This approach appears particularly relevant for this group given that child challenging behaviour was identified as a predictor of stress in the present study (see Table 12.2). The recognition of the children's ASD characteristics may help to ensure that relevant programmes are put in place. As discussed in Chapter 6, Section 6.6.8, specific programmes have been developed for children with ASD. For instance, the Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH; Mesibov et al., 2004) programme has been widely adopted in the UK and attendance at TEACCH programmes has been shown to reduce depression in parents (Bristol, Gallagher & Holt, 1993).

The implementation of a specific support network for parents of children with DS and co-morbid ASD (in addition to the Down's Syndrome Association (DSA) which all participants were active members of) may also have positive effects (see Chapter 12, Section 12.4 for further discussion). The support networks provided by ASD support organisations (such as the National Autistic Society) might also be developed further for this group.

13.5 Suggestions for future research

Longitudinal study

Although the present study provides a useful picture of the behavioural phenotype of DS and co-morbid ASD during childhood, behavioural phenotypes can vary according to chronological age. Chapman and Hesketh (2000) reviewed the literature on the behavioural phenotype of DS and noted that differences were observed across the lifetime. For instance, fewer maladaptive behaviours are reported in young adults with DS compared with children, and symptoms of dementia can emerge in later adulthood for a considerable number of individuals with DS (Chapman & Hesketh, 2000). Although it must be noted that Carr (2012), who followed a group of individuals with DS from 6 weeks to 45 years, highlighted the maintenance of some skills through adulthood, namely verbal intelligence and self-help skills. As like in DS, variation in the presentation of ASD across the lifetime has been reported (Esbensen et al., 2009; Howlin et al., 2013). Some previous studies in

the field of DS and co-morbid ASD have used samples spanning infancy to adulthood which was flagged up as a concern because of the possible variation in the behavioural phenotype across the lifetime (see Chapter 3). A longitudinal study following individuals with DS and co-morbid ASD over time could help determine whether chronological age affects the presentation of challenging behaviours, ASD characteristics and the stability of the ASD diagnosis in this group.

Evaluation of alternative screening tools

Both the SCQ and the DBC-ASA were found to be adequate tools when screening for ASD in children with DS. However, data from these questionnaires in the current sample indicated that the tools may be less reliable in children with DS than individuals with idiopathic ASD (Charman et al., 2007; Witwer & Lecavalier, 2007). The SCQ has been the dominant screening questionnaire in ascertaining the prevalence of ASD in the DS population (DiGuiseppi et al., 2010; Lowenthal et al., 2010; Magyar et al., 2012; Moss et al., 2013b); however, there are other tools that may prove more effective. The Social Responsiveness Scale (SRS; Constantino & Gruber, 2002), for instance, is a parent and teacher completed questionnaire with 65 items rated on a 4-point Likert scale (from 'not true' to 'almost nearly true') also widely used in screening for ASD. However, it appears to be less effective in screening samples of low IQ (Charman et al., 2007).

A more promising tool which was specifically designed for the detection of ASD in individuals with intellectual disability is the Pervasive Developmental Disorder in Mental Retardation Scale, second edition (PDD-MRS; Kraijer, 2006). The PDD-MRS is a questionnaire with 12 items rated in terms of presence (+) or absence (-). The manual states that with individuals with DS sensitivity and specificity rates of .90 and .88 respectively have been achieved (Kraijer, 2006). Ethical approval was granted for the measure to be added to the present study (see Appendix C); however, the measure was not included in analyses because of a vast amount of missing data (i.e. 18 forms not completed). Several parents made comments about the measure being difficult to understand. The measure was originally created in Dutch and has been translated into English. The language is somewhat formal, for example it asks whether social interaction is "consonant" with levels of functioning. Moreover, the 12 items are divided into 4 sections, each of which has a different coding system. A further research study could consider modifying the PDD-MRS to improve its accessibility for parents in the UK, as well as evaluating it against other screening tools such as the SRS.

Qualitative assessment of the barriers to diagnostic assessment

Previous research has indicated that many parents of children with DS experience major difficulties in obtaining an autism diagnostic assessment (Patterson, 1999). The evaluation of the nature of comments made by respondents about seeking a diagnosis in the questionnaire survey of the present study (see Chapter 6, Section 6.5.1) supported the notion that the process can be difficult for some. Such findings call for a more detailed assessment of the barriers to attaining an assessment, with information being needed from both clinicians and parents regarding the difficulties faced by both parties and ways in which these might be overcome.

Investigation of the impact of hearing impairment

An association between the reported presence of a hearing impairment and misclassification by the SCQ was found in the present study (see Chapter 11, Section 11.3, p.175). This has clear implications for the screening process. However, the sample of children with a hearing impairment was very small (n=9). To further elucidate the impact of hearing impairment on screening for ASD in children with DS, a larger scale study with hearing impairment as a primary focus could be conducted.

Further investigation into the function of challenging behaviours

In the present study, the Questions about Behavioural Function-Modified (QABF-M) was utilised only in relation to the behaviour the parent found "most challenging". Although this gives some insight into the function of challenging behaviour for children with DS and co-morbid ASD, the utilisation of the measure for each form of challenging behaviour would give a better indication of which specific interventions to recommend to parents.

The natural observation identified that stereotyped behaviours were more commonly demonstrated by children in the DS+ASD group than children in the DS-only group and that an unstructured environment may be involved in the function of such behaviours. Functional analysis through an experimental design may add to these findings (see Horsler & Oliver, 2006; Arron et al., 2006 for examples). Experimental manipulations could be used to further explore what aspects of an unstructured environment may lead to increases in stereotyped behaviours. Possible explanations include a lack of demand, or a lack of attention. Moreover, rather than broadly defining stereotyped behaviour (as in the present study), the specific topographies of stereotyped behaviour could be recorded.

Sensory processing

In evaluating the higher rates of stereotyped behaviour in the DS+ASD group a possible connection with sensory processing difficulties was postulated (see p.157-158). This hypothesis could be examined by the utilisation of sensory processing measures, not only in children with DS and co-morbid ASD but also within DS-only groups, as a literature search highlighted the lack of research into sensory processing in DS more generally.

Family background

As noted in the discussion of the study limitations (Section 13.2.2), a more comprehensive evaluation of family background would enhance knowledge of the impact on the family of raising a child with DS and co-morbid ASD. Information about the presence of ASD characteristics in other family members is also of potential importance and Rasmussen et al. (2001) suggested that a history of autistic disorder in relatives is a factor associated with DS and co-morbid ASD. Several researchers have explored autistic traits in parents of children with ASD. The Broader Autism Phenotype (BAP), a set of behaviours qualitatively similar to ASD, has been identified in relatives of individuals with ASD and is thought to suggest genetic liability of ASD (see Chapter 2, Section 2.4.1 for further information on the genetic factors related to ASD). The BAP has also been associated with parental stress and depression (Ingersoll & Hambrick, 2011). Therefore, the utilisation of a BAP measure with this group might prove valuable. Another factor that has been linked to the aetiology of ASD is advancing parental age (see Chapter 2, Section 2.4.1). The relevance of parental age may be greater in the case of DS and co-morbid ASD given that advancing maternal age is strongly linked to the aetiology of DS.

13.6 Final conclusions

This study is the largest survey to screen children with Down syndrome (DS) for autism spectrum disorder (ASD) characteristics. It is also the first systematic study to consider the autism profile of children with DS in depth, to consider the school environment when evaluating challenging behaviour in children with DS and co-morbid ASD, and to consider individual variability within the group. Moreover, it is the first to systematically consider the impact on the family of raising a child with DS and co-morbid ASD.

The findings indicate that a substantial proportion of children with DS screen positive for ASD, but also that subtle differences are evident in the presentation of ASD in this group compared with idiopathic ASD. When compared with children with DS only,

this group reportedly demonstrate poorer communication and adaptive behaviour skills and increased levels of challenging behaviour. However, challenging behaviour profiles may vary between home and school with parents and teachers reporting somewhat different difficulties. An exception is stereotyped behaviours, which appear to be pervasive in this group. Although these findings help to establish a behavioural phenotype of the co-morbidity, individual differences were also noted. A further finding was that parents of children with DS and co-morbid ASD report greater stress than parents of children with DS only, and that child challenging behaviour is a sound predictor of the reported stress.

Combined, these findings have enhanced our understanding of DS and co-morbid ASD. They should go some way towards improving awareness and clinical practice. What is more, they have alerted us to the fact that behavioural intervention is needed in this group, not only to improve child outcomes but also to reduce stress experienced by parents.

Can we conclude that rates of ASD are raised in children with Down syndrome?

First, it is important to note that establishing rates of ASD is problematic - whether one seeks to establish the rate of ASD in a genetic syndrome such as DS, or more generally in the wider population. There has been a continued rise in ASD prevalence estimates, which could represent a true prevalence increase or reflect an increased awareness of the disorder. Moreover, recent data reported by the Center for Disease Control and Prevention shows marked differences for one area to another (CDC, 2014). As reported in Chapter 6, the present study (as like most studies of this kind) was potentially subject to sampling bias and/or affected by a potential shift in participant knowledge as well as statistical power. All of the aforementioned factors can lead to disparity between reports of prevalence estimates.

The belief that DS is rarely associated with autism (Rutter & Hersov, 1985) is still common among many clinicians and has also influenced researchers' understanding of the co-morbidity. Thus, research studies in this area tend to be based on the premise that ASD and DS should co-occur at or below the rate in the general population (i.e. it is expected that around 1% or less of individuals with DS will have ASD).Based on this premise, the present study clearly indicates an elevated risk of ASD in children with DS in England and Wales.

However, this interpretation does not take into account the high rate of intellectual disability (ID) in children with DS (Hodapp, 1999). Reports indicate that between 4-40% of individuals with ID display characteristics of ASD (Matson & Shoemaker, 2009).The proportion of children with DS meeting the screening threshold for ASD in the present

study (37.7%) implies that rates of ASD in DS are no greater than would be expected based on the level of ID in this group. If one were to consider this rate inflated (as discussed in Chapter 6), and the true rate to lie closer to 20% (as implied by the epidemiological model outlined in this thesis), then one could argue that DS in fact confers some kind of 'protective factor' with respect to ASD. Indeed, comparison across reported rates of ASD in other genetic disorders indicates that the prevalence in DS could be lower than other disorders (e.g. Tuberous Sclerosis Complex and Angelman syndrome).

It is clear that establishing the true rate of ASD in DS requires not only much larger, epidemiological samples, but also measures of ASD that are fully validated for children with other genetic and/or developmental disorders. These remain major challenges for the future. Nevertheless, in contrast to Rutter and Hersov's suggestion that the two conditions rarely co-occur, the present study indicates that the association between the two is far from unusual (whether or not it is higher or lower than one should 'expect') and awareness of this has important implications. For instance, attainment of the dual diagnosis may help a child to attend a more appropriate school or may help parents to better understand why their child with DS is so different from the characteristic stereotype.

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List of appendices

Appendix A

Publication:

Warner, G., Moss, J., Smith, P. & Howlin, P. (2014) Autism Characteristics and Behavioural Disturbances in ~500 Children with Down Syndrome in England and Wales, *Autism Research*

RESEARCH ARTICLE

Autism Characteristics and Behavioural Disturbances in ~ 500 Children with Down's Syndrome in England and Wales

Georgina Warner, Joanna Moss, Patrick Smith, and Patricia Howlin

Recent research shows that a significant minority of children with Down's syndrome (DS) also meet diagnostic criteria for an autism spectrum disorder (ASD). The present study investigated what proportion of children aged 6–15 years with a confirmed diagnosis of DS in England and Wales display autistic-type behaviours, and explored the characteristics of this group of children. The Social Communication Questionnaire (SCQ) was used to screen for autism characteristics and the Strengths and Difficulties Questionnaire (SDQ) to explore behavioural difficulties. The proportion of children who met the cut-off score for ASD on the SCQ (total score ≥ 15) was 37.7% (95% CI: 33.4–42.0%); for autism (total score ≥ 22) the proportion was 16.5% (95% CI: 13.2–19.8%). Children who met the cut-off for ASD were significantly more likely to be reported as having emotional symptoms, conduct problems and hyperactivity on the SDQ than children who scored well below cut-off (total score < 10). However, the profile of their autism characteristics on the SCQ was atypical compared with individuals with idiopathic ASD. The pervasiveness of ASD in children with DS in England and Wales is substantially higher than in the general population. These children also experience significantly greater behavioural problems than children with DS only. Early detection of autism characteristics is important for appropriate intervention. However, the unusual profile of autism characteristics in this group may affect the recognition of the disorder and hinder the implementation of appropriate interventions. ***Autism Res*** *2014, ••: ••–••.* © 2014 International Society for Autism Research, Wiley Periodicals, Inc.

Keywords: autism spectrum disorder; Down's syndrome; social communication questionnaire; strengths and difficulties questionnaire

Introduction

The association between autism spectrum disorders (ASD) and other genetic syndromes has been widely researched over recent years. For example, Fragile X syndrome [Hall, Lightbody, Hirt, Rezvani, & Reiss, 2010] and tuberous sclerosis complex [Numis et al., 2011] are but two of the many genetic syndromes in which autistic-like characteristics have been reported [Moss, Howlin, & Oliver, 2011]. Despite the early view that Down's syndrome (DS) was rarely associated with autism [Rutter & Hersov, 1985], more recent research indicates that a significant minority of individuals with DS meet diagnostic criteria for an ASD. DS is the most common chromosomal cause of intellectual disability (ID) and occurs in approximately 1.08 per 1000 live births [Morris & Alberman, 2009]. It is caused by abnormal cell division involving chromosome 21 (Trisomy 21, Mosaicism and Translocation) [Wiseman, Alford, Tybulewicz, & Fisher, 2009]. Trisomy 21 is the most common cause, affecting around 95% of individuals with DS [Morris & Alberman, 2009].

Although case studies of ASD in individuals with DS emerged some years ago [e.g. Ghaziuddin, Tsai, & Ghaziuddin, 1992; Howlin, Wing, & Gould, 1995], systematic investigation of autism characteristics in DS has only developed in recent years. Using the Social Communication Questionnaire [SCQ; Rutter, Bailey, & Lord, 2003], a well-standardised screening tool for autism characteristics, it has been estimated that around 16% [sample size = 180, Lowenthal, Paula, Schwartzman, Brunoni, & Mercadante, 2007], 18% [sample size = 123, DiGuiseppi et al., 2010] or 19% [sample size = 108, Moss, Richards, Nelson, & Oliver, 2013b] of individuals with DS pass the screening threshold for ASD. This indicates a highly elevated risk compared with the general population, in whom the risk is around 1% [Baird et al., 2006]. However, these figures need to be treated with caution given the limited sample sizes and the localised geographical sampling methods adopted by these studies.

Investigation into the phenotypic characteristics of individuals with DS and ASD indicates elevated levels of behavioural disturbances, when compared with

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individuals with DS only [Capone, Grados, Kaufmann, Bernad-Ripoll, & Jewell, 2005; Ji, Capone, & Kaufmann, 2011]. In particular, individuals with DS and ASD tend to show increased rates of stereotyped behaviours, overactivity, impulsivity and self-injurious behaviour [Moss et al., 2013b]. Severity of ID is also greater in individuals with DS and ASD than in individuals with DS only [Capone et al., 2005; Carter, Capone, Gray, Cox, & Kaufmann, 2007; Molloy et al., 2009]. Relatively higher rates of language deficits, both expressive and receptive, and language regression have been reported in children with DS and ASD [Molloy et al., 2009]. Regression in more general skills has also been noted [Castillo et al., 2008].

The present study is the first to assess the rates of autism characteristics in children with DS across England and Wales. The specific autism profile of children with DS who meet the screening threshold for ASD is compared with that of an idiopathic ASD reference group [Berument, Rutter, Lord, Pickles, & Bailey, 1999]. Behavioural disturbances, communication problems and incidence of regression are also compared between children with DS who meet the screening threshold for ASD and those who score well below threshold.

The study aimed to answer the following research questions:

1. What proportion of children (aged 6–15 years) with a confirmed diagnosis of DS in England and Wales meet cut-off scores for ASD (total score ≥ 15) and autism (total score ≥ 22) on the SCQ?
2. What is the gender ratio of children who meet cut-off scores?
3. Among children with DS who meet the cut-off for ASD on the SCQ and those who score well below cut-off (total score < 10), how does the profile of ASD characteristics differ from that of individuals with idiopathic ASD (i.e. from the ASD reference group)?
4. Do children with DS who meet the SCQ cut-off for ASD show a specific pattern of general behaviour problems, as measured by the Strengths and Difficulties Questionnaire [SDQ; Goodman, 1997], compared with those who score well below cut-off?
5. Do children with DS who meet the SCQ cut-off for ASD show greater communication problems and a higher rate of developmental regression than those who score well below cut-off?

Method

Participants

The families of children with a confirmed diagnosis of DS, aged between 6 and 15 years, who resided in England or Wales were recruited via the UK Down's Syndrome Association and asked to take part in a study of differences among children with DS. In total, 1382 families were contacted. Of these, 507 individuals (36.7%) returned the questionnaires. Eight participants (1.6%) were excluded from the study because they did not provide information regarding the child's date of birth or the child was outside the age range of the study. This left a total sample of 499 participants.

A group of 160 individuals with Pervasive Developmental Disorder (PDD) from a previous study reported in the SCQ manual [Berument et al., 1999] was used as an ASD reference group for the analysis of the autism profile of children with DS. Although this is an established method of comparison [Hall et al., 2010; Moss, Oliver, Nelson, Richards, & Hall, 2013a], it was not possible to match the ASD reference group directly with the DS group. In particular, the age range of the ASD group was wider (4–40 years *versus* 6–15 years) which may have some implications for comparability.

Measures

Lifetime version of the Social Communication Questionnaire [SCQ; Rutter et al., 2003]. The SCQ is a 40-item parent report screening measure that identifies characteristics associated with ASD. Each item is dichotomous and scored to indicate the presence (score = 1) or absence (score = 0) of the autism characteristic; severity of behaviour is not rated. The items can be divided into three subdomains: Reciprocal Social Interaction, Communication, and Restricted, Repetitive and Stereotyped Patterns of Behaviour. The Lifetime version of the questionnaire refers to the entire developmental history of the child. Item level validity is good, with 31 out of 39 items significantly differentiating individuals with ASD from those without [Berument et al., 1999; Bölte, Holtmann & Poustka, 2008]. The recommended ASD cut-off of 15 was found to differentiate individuals with PDD from other diagnoses, even in the case of individuals with ID where specificity was reported at 0.67 and sensitivity at 0.96. Magyar, Pandolfi, and Dill [2012] conducted a psychometric evaluation of the SCQ in a sample of children with DS and concluded that the screening tool is suitable for use with this group. The measure, and the recommended cut-off of 15, was found to be reliable and to accurately categorise the children according to whether they had co-morbid ASD or not [Magyar et al., 2012].

Strengths and Difficulties Questionnaire [SDQ; Goodman, 1997]. The SDQ is a 25-item screening measure for the psychological adjustment of children and youths. It generates scores for emotional symptoms, conduct problems, hyperactivity, peer problems and prosocial behaviour. A study evaluating the psychometric properties of the SDQ [Goodman, 2001] concluded that

the parent form had good internal consistency, with Cronbach α coefficients ranging from 0.57 to 0.85 across the subdomain, total and impact scores.

General Information Questionnaire

A General Information Questionnaire was created in order to obtain further information about the development and demographics of the children. The questions covered areas such as communication methods, regression in language and general skills, genetic mechanism of DS and closest town or city.

English Indices of Deprivation (2007)

The socioeconomic status of survey respondents was assessed using the English Indices of Deprivation Report (Office for National Statistics, 2007). This includes factors such as income, employment, health, education, barriers to housing and services, living environment and crime. These elements are weighted and combined to form a deprivation index; each district in England is labelled according to the decile in which it scores. Each respondent was assigned a numerical value of 1 (most deprived) to 10 (least deprived) according to the percentile of the district in which they lived. Deciles 1, 2 and 3 were grouped to form the "most deprived" areas, deciles 4, 5, 6 and 7 the "moderately deprived", and 8, 9 and 10 the "least deprived." Respondents who did not specify their location with adequate detail were excluded from this analysis ($n = 37$), as were individuals living in Wales as information on Welsh districts was not available ($n = 22$).

Data Analysis

For comparative analyses, children who met the ASD cut-off (total SCQ score ≥ 15) were referred to as the DS + ASD group ($n = 183$); children who scored well below cut-off on the SCQ (total score < 10) were referred to as the DS-only group ($n = 190$) (see Table 1 for group characteristics). A total score of 10 was taken as the lower-cut point as it lies below the basal score that has been identified as useful in the detection of ASD [cut-off = 11, Eaves, Wingert, Ho, & Mickelson, 2006]. Furthermore, Magyar et al. [2012] reported a mean SCQ total score of 9.13 (SD = 6.33) for a DS-only group. Although this sampling strategy should provide a group representative of children with DS only, it must be noted that type II errors are still possible given the imperfect sensitivity rates of the SCQ. The PDD group from the SCQ manual were referred to as the ASD reference group.

The proportion of individuals with DS meeting cut-off on the SCQ was calculated using SCQs that were at least 75% complete at the subdomain level ($n = 485$). Missing data on these forms were replaced with mean subdomain scores. All data were tested for normality using Kolmogorov–Smirnov tests. Mann–Whitney *U*- and Chi-square tests were used to evaluate differences between the DS + ASD group and the DS-only group.

Table 1. Age, Gender, Verbal Ability and SCQ Total Scores for the DS Total Group (With Complete SCQ Data), DS + ASD Subsample and DS-Only Subsample

		DS total group (with SCQ data)	DS + ASD	DS-only
N		485	183	189
Age	Mean (SD)	10.43 (2.77)	10.87 (2.78)	10.10 (2.80)
	Range	6.00–15.00	6.00–15.00	6.00–15.00
Gender	% male (*N*)	56.29 (273)	67.21 (123)	47.62 (90)
Verbal[a]	%verbal (*N*)	93.40 (453)	79.23 (145)	98.41 (186)
SCQ score	Mean (SD)	13.12 (7.73)	21.33 (5.34)	5.89 (2.44)
	Range	0.00–36.00	15.00–36.00	0.00–9.00

[a]Able to use phrase/sentence speech or single words to communicate according to parent reports on the General Information Questionnaire.

Odds ratios (and 99% confidence intervals) were calculated to determine SCQ item-specific differences between the DS + ASD and DS-only groups and the ASD reference group [Hall et al., 2010; Moss et al., 2013a]. The numbers of children in each group who scored on an individual SCQ item, and thus displayed the "autism characteristic", were used to calculate odds ratios. An odds ratio significantly above 1.0 was taken to indicate that the autism characteristic was significantly more likely to be present in the DS + ASD (or DS-only) group than the ASD reference group. An odds ratio significantly less than 1.0 was taken to indicate that the autism characteristic was significantly less likely to be present in the DS + ASD (or DS-only) group than the ASD reference group. The conclusions refer only to the likelihood of an impairment being noted by the parents, not to the severity of impairment. Items were regarded as significant if the value of 1.0 lay outside of the 99% confidence interval for that item. A second odds ratio analysis excluding non-verbal children was run for the "social chat" item on the communication domain as this item, unlike others at the beginning of the SCQ form, was not subject to verbal ability screening.

A proportional SCQ communication score was derived for those children who were non-verbal in order to ensure that general communication difficulties were comparable across groups. Eaves et al. [2006] used a similar strategy. The proportional communication score was derived using the following calculation: (Sum of domain items completed ÷ Number of domain items completed) × 13.

The mean score is multiplied by thirteen as there are thirteen items in the communication domain. Although, using this transformation, the majority of scores remained unchanged or changed by less than one point

($n = 407$), 78 (16%) were changed by more than one point. The greatest point difference was five ($n = 22$).

Results

Sample Details

Of the total DS sample ($n = 499$), 281 (56%) were male and 218 (44%) were female. Of the participants whose parents knew the genetic mechanism of the DS ($n = 460$), 437 (95%) had Trisomy 21, 12 (3%) Mosaicism and 11 (2%) Translocation. According to parental reports on the General Information Questionnaire ($n = 496$), 377 (76%) of the children were able to talk using phrases or sentences, 76 (15%) communicated using only single words and 43 (9%) were non-verbal. The verbal ability of the subgroups (i.e. DS + ASD and DS-only) is presented in Table 2.

Responses were received from locations all over England and Wales. The application of population-weighted district level averages of deprivation [Office for National Statistics, 2007] to participants who resided in England and provided their local town or city ($n = 440$), indicated that the sample was evenly distributed in terms of socioeconomic status when grouped into the most deprived (36%), moderately deprived (32%) and least deprived (32%).

Research Questions

1. *What proportion of respondents meet cut-off scores for ASD and autism on the SCQ?*

The proportion of children who met the cut-off score for ASD on the SCQ (total score ≥ 15) was 37.7% (95% confidence interval [CI]: 33.4–42.0%) and for autism (total score ≥ 22) 16.5% (95% CI: 13.2–19.8%).

2. *What is the gender ratio of those children who meet cut-off scores on the SCQ?*

Of the children who met the cut-off for ASD (total score ≥ 15) on the SCQ ($n = 183$), 123 (67%) were male and 60 (33%) were female (χ^2 (1, $N = 485$) = 14.26, $P < .001$; OR = 2.1). Of those who met the autism cut-off (total score ≥ 22; $n = 80$), 60 (75%) were male and 20 (25%) were female, (χ^2 (1, $N = 485$) = 13.63, $P < .001$; OR = 2.7).

3. *How do SCQ profiles differ between the two groups and the ASD reference group?*

Communication domain. Children in the DS + ASD group were significantly *less* likely to be impaired than the ASD reference group on three items in the Communication domain: imitation (OR = 0.3), use of gestures (OR = 0.5) and imitative social play (OR = 0.3). Conversely, they were *more* likely to be impaired than the ASD reference group on pronoun reversal (OR = 4.5), using neologisms (OR = 2.2) and social chat (OR = 16.9) (see Fig. 1).

The DS-only group were significantly *less* likely to be impaired than the ASD reference group on most items in the Communication domain. However, similar proportions of parents in the DS-only and ASD reference groups reported the use of neologisms (OR = 1.0) and an impairment in social chat (OR = 1.1). The DS-only group were significantly *more* likely than the ASD reference group to reverse their pronouns (OR = 1.8).

Table 2. Verbal Ability of DS + ASD and DS-Only Children, as Reported on the General Information Questionnaire

Verbal Ability	Group	% (*N*)
Phrase/sentence speech	DS + ASD	57 (103)
	DS-only	90 (169)
Single words only	DS + ASD	23 (42)
	DS-only	9 (17)
Non-verbal	DS + ASD	20 (37)
	DS-only	1 (2)

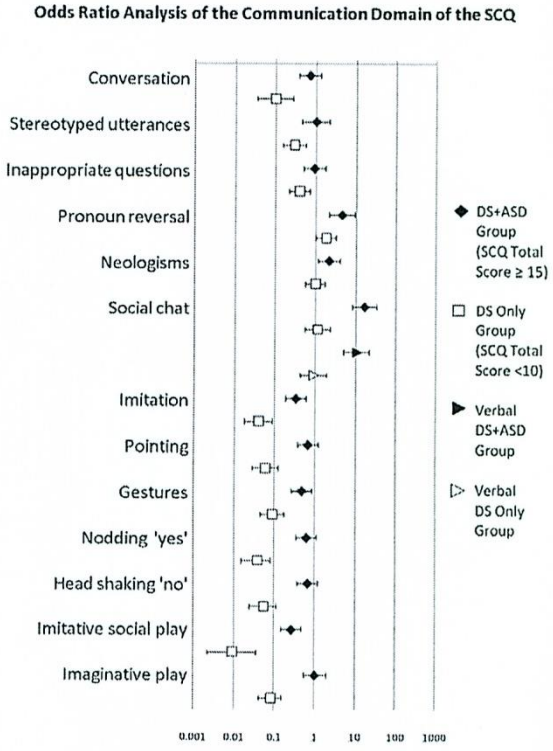

Figure 1. Odds ratio analysis of communication items on the SCQ, comparing DS + ASD and DS-only groups with an ASD reference group.

When non-verbal children were excluded from the odds ratio, children in the DS + ASD group remained significantly *more* likely to be impaired in social chat than the ASD reference group (OR = 10.7), and the proportions of children reported to show an impairment in social chat remained similar in the DS-only and ASD reference groups (OR = 0.9).

Reciprocal Social Interaction domain. Children in the DS + ASD group were significantly *less* likely than the ASD reference group to be impaired on the following 6 items: eye gaze (OR = 0.5); social smiling (OR = 0.5); shared enjoyment (OR = 0.5); offering comfort (OR = 0.3); social overtures (OR = 0.5) and response to other children's approaches (OR = 0.4) (see Fig. 2). No social interaction deficits, as measured by the SCQ items, were found to be statistically *more* likely to be present in the DS + ASD group than the ASD reference group.

The DS-only group were significantly *less* likely to be impaired than the ASD reference group on *all* items in the Reciprocal Social Interaction domain (inappropriate facial expressions, OR = 0.2; use of other's body, OR = 0.3; friends, OR = 0.1; imaginative play with peers, OR = 0.1). The odds ratios for the remaining items were all less than 0.1, except social smiling for which an odds ratio could not be calculated as none of the children in the DS-only group showed impairment in this area.

Restricted, Repetitive and Stereotyped Patterns of Behaviour domain. Only one item (compulsions and rituals) in the Restricted, Repetitive and Stereotyped Patterns of Behaviour domain significantly distinguished between the DS + ASD group and ASD reference group (OR = 2.9; see Fig. 3). No SCQ items in this domain were found to be statistically *less* likely to be present in the DS + ASD group than the ASD reference group.

The DS-only group were significantly *less* likely to be impaired than the ASD reference group on *all* items in the Restricted, Repetitive or Stereotyped Patterns of Behaviour domain (verbal rituals, OR = 0.1; compulsions and rituals, OR = 0.4; repetitive use of objects, OR = 0.1; circumscribed interests, OR = 0.2; unusual sensory inter-

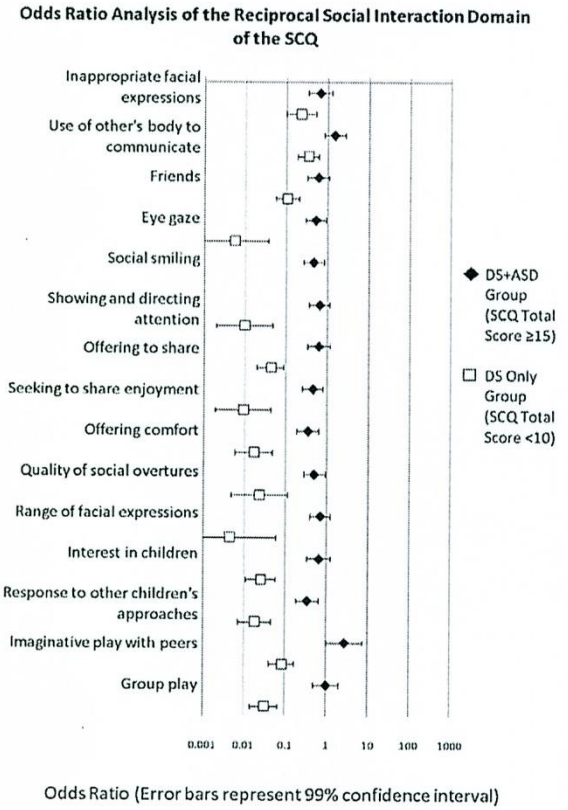

Figure 2. Odds ratio analysis of reciprocal social interaction items on the SCQ, comparing DS + ASD and DS-only groups with an ASD reference group.

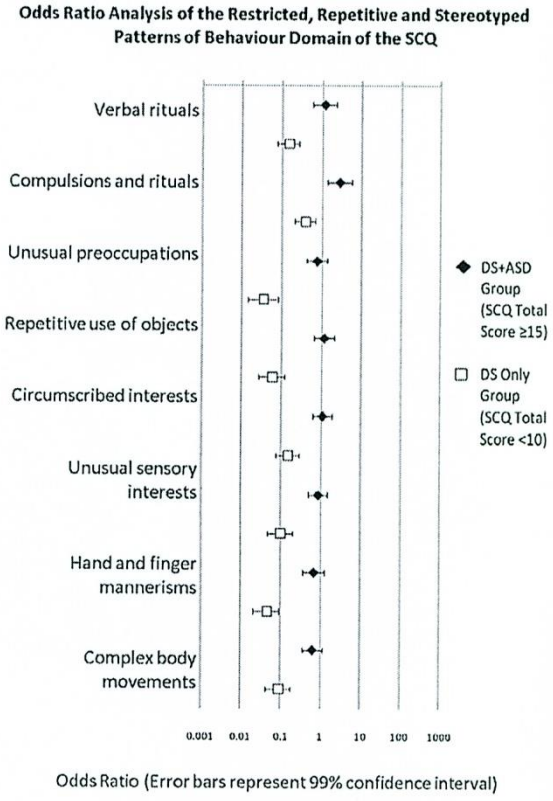

Figure 3. Odds ratio analysis of restricted, repetitive and stereotyped patterns of behaviour items on the SCQ, comparing DS + ASD and DS-only groups with an ASD reference group.

Table 3. Strengths and Difficulties Questionnaire Normal Score Range, DS + ASD and DS-Only Group Average Scores, and Group Differences as Measured by Mann–Whitney *U*-Tests

SDQ Subdomain[a]	Group	Median	Mann-Whitney z	Sig.	Cohen's r (Effect Size)
Emotional symptoms	DS + ASD	3			
(Normative mean = 1.9)	DS-only	1	5.48	< .001	0.29 (Medium)
Conduct problems	DS + ASD	3			
(Normative mean = 1.6)	DS-only	2	5.96	< .001	0.31 (Medium)
Hyperactivity	DS + ASD	7			
(Normative mean = 3.5)	DS-only	4	8.15	< .001	0.42 (Large)
Peer problems	DS + ASD	5			
(Normative mean = 1.5)	DS-only	2	9.59[b]	< .001	0.50 (Large)
Prosocial behaviour	DS + ASD	5			
(Normative mean = 8.6)	DS-only	8	−10.64[b]	< .001	0.55 (Large)

[a]Mean scores for normative sample (ages 5–15) in parenthesis.
[b]Conclusions to be treated with caution as the homogeneity of variance assumption has been violated.

ests, OR = 0.1; complex body mannerisms, OR = 0.1). The odds ratios for the remaining items were less than 0.1.

4. *Do children with DS who meet the SCQ cut-off for ASD show a specific profile of general behaviour problems compared with those scoring well below cut-off?*

The DS + ASD group was reported to experience significantly more emotional symptoms, conduct problems, hyperactivity and peer problems and display significantly less prosocial behaviour than the DS-only group (See Table 3). However, conclusions drawn from the group comparisons of peer problems and prosocial behaviour must be treated with caution as the homogeneity of variance assumption was violated for these two subdomains.

5. *Do children with DS who meet the SCQ cut-off for ASD show greater communication problems and a higher rate of developmental regression than those scoring well below cut-off?*

According to parental reports on the General Information Questionnaire, children in the DS + ASD group were significantly less likely than children in the DS-only group to be able to communicate using phrases and sentences (χ^2 (1, N = 370) = 52.67; OR = 0.6) (see Table 2).

On average, among children who were verbal, those in the DS + ASD group acquired language significantly later (36.6 months, SD = 18.7) than children in the DS-only group (30.3 months, SD = 12.8) (z = 3.98, $P < .001$, Cohen's r = 0.23).

Children in the DS + ASD group were significantly more likely to be reported as having general communication problems, on the SCQ adjusted communication domain score, than the DS-only group (z = 15.08, $P < .001$, Cohen's r = 0.78).

Children in the DS + ASD group were more likely to be reported as having lost *language* skills than those in the DS-only group (χ^2 (1, N = 363) = 42.61, $P < .001$; OR = 4.5). Children in the DS + ASD group were also significantly more likely than the children in the DS-only group to have a reported loss in *general* skills (χ^2 (1, N = 362) = 40.57, $P < .001$; OR = 4.8).

Discussion

Main Findings

The proportions of children with DS meeting the SCQ cut-off for ASD and autism were 37.7% ($n = 183$) and 16.5% ($n = 80$) respectively. The proportion of males meeting the ASD cut-off was significantly greater than the proportion of females.

Compared with the ASD reference group, children in the DS + ASD group were less likely to be reported as showing impairment in several aspects of non-verbal communication on the SCQ including use of gesture, imitation or imitative social play. However, they were more likely to be reported as showing impairments in areas such as pronoun reversal, use of neologisms and social chat. Impairments in these latter three areas were also more frequent in the DS-only group than the ASD reference group. Possible reasons for these unexpected findings are described below.

In terms of reciprocal social interactions, children in the DS + ASD group were *less* likely than the ASD reference group to be reported as showing impairments on most SCQ items in this domain suggesting that the relatively high level of social competence typically displayed by individuals with DS [Rosner, Hodapp, Fidler, Sagun, & Dykens, 2004] may act as a form of "buffer" to the social deficits seen in ASD. Conversely, children in the DS + ASD group were reported to show a greater tendency to exhibit compulsions or rituals than the ASD reference group.

On the SDQ, children in the DS + ASD group were reported to show significantly more emotional symptoms, conduct problems and hyperactivity than children in the DS-only group. They also showed poorer general

communication skills and were less likely to use verbal communication. Of those who did have language, children in the DS + ASD group were reported to have acquired their first words at a later age than children in the DS-only group.

Findings Consistent with Previous Literature

The high level of hyperactivity reported in the DS + ASD group replicates findings from previous studies [Capone et al., 2005; Moss et al., 2013b]. The higher level of conduct problems, too, is consistent with previous reports of increased disruptive behaviour in individuals with DS and ASD [Ji et al., 2011], and the higher level of emotional symptoms reflects previous reports of increased anxiety in this group [Carter et al., 2007]. The deficits in communication are consistent with previous research, noting poorer receptive and expressive language in children with Trisomy 21 and ASD [Molloy et al., 2009].

Conflicting Findings

The proportions of participants meeting cut-off for ASD on the SCQ are elevated when compared with previous prevalence estimates generated by the same screening tool [Lowenthal et al., 2007; Moss et al., 2013b]. This difference may be due to sample characteristics or sample size, as the current sample is younger and much larger than those in previous studies. It is also possible that parents in the present study are now more aware of autism characteristics and the possible co-occurrence with DS than parents of older cohorts.

The fact that children in both the DS + ASD *and* DS-only groups showed more impairments than the ASD reference group in certain aspects of verbal communication (e.g. use of personal pronouns, neologisms and social chat) was particularly unexpected. A previous investigation of expressive language in adolescents and young adults with DS found no difference in the use of personal pronouns when compared with a typically developing group [Finestack & Abbeduto, 2010]; moreover, many individuals with DS typically enjoy talking to others. The reasons for these discrepancies are unclear, but it should be noted that the validity of the pronoun reversal and neologism items in screening for ASD is debatable as these items were among those that failed to differentiate between individuals with/without ASD [Berument et al., 1999]. It is also possible that parents of children with DS may, in some way, have misinterpreted the SCQ question about social chat, ("Does she/he ever talk with you just to be friendly?") particularly as on most other items related to reciprocal social interactions, the ASD reference group were more likely to be rated as showing impairments.

The increased likelihood of compulsions and rituals in the DS and ASD group is also inconsistent with previous findings which reported no significant differences between DS / DS + ASD / ASD groups on compulsive behaviour, insistence on sameness or restricted preferences [Moss et al., 2013b]. Again, this may be due to differences in sample characteristics as the comparison groups in the Moss *et al.* study were small ($n = 17$) and participants' age ranged from 4 to 43 years.

Finally, in the present study, the proportion of males to females in the DS + ASD group is greater than reported by Lowenthal et al. [2007] and Moss et al. [2013b], and DiGuiseppi et al. [2010] found no gender differences. However, the gender ratio reported here is not dissimilar to that found in idiopathic ASD, where a male to female ratio of 4:1 is typical [Fombonne, 2003].

Limitations of the Study

There are a number of limitations associated with this study that restrict the conclusions that can be drawn.

First, all the data were attained through informant measures and there was no direct assessment of the children themselves. Such reliance on parent reports created the opportunity for misinterpretation of items. Direct assessment of the children (e.g. administration of the Autism Diagnostic Observation Schedule-Generic [ADOS-G; Lord et al., 2000] and/or the Autism Diagnostic Interview-Revised [ADI-R; Rutter, LeCouteur, & Lord, 2003]) would have provided more valid measures of ASD characteristics, allowing for more robust groupings and a more effective analysis of the autism profile. However, the selected measures are of a high standard; the SCQ has been reported in previous studies as having good convergent validity with ASD diagnostic assessments, specifically when used with individuals with DS [Magyar et al., 2012], and the SDQ has good internal consistency and is widely used in clinical settings. Moreover, time and resources did not permit the direct assessment of such a large sample.

Second, this cannot be considered as an epidemiological study as participant families were volunteers recruited through the Down's Syndrome Association; however, the demographics of the sample were evenly spread and therefore representative of the wider population in terms of gender and socioeconomic status. Furthermore, the proportions of participants with each genetic mechanism of DS reflected those of the DS population [Freeman et al., 2007]. Although fairly low, the response rate of 36% exceeded that of previous studies [DiGuiseppi et al., 2010; Moss et al., 2013b] and this is the largest sample size in a study of this kind.

Finally, the DS groups were not matched to the ASD reference group. Intelligence Quotient (IQ) measures were not utilised in either study, but the IQ of the DS groups was likely to be lower. Furthermore, the ASD reference group included some adults. Differences such as these may clearly have affected conclusions.

Implications of Findings

The study has important implications for the recognition of ASD in children with DS and the implementation of appropriate interventions. The high number of children passing the screening threshold for ASD should raise awareness of the potentially higher risk of co-morbidity between the two conditions. It has been noted that making the dual diagnosis is difficult and, if achieved, tends to come late in childhood, often during adolescence [Rasmussen, Borjesson, Wentz, & Gillberg, 2001]. Increased awareness of the possible association between DS and ASD should lead to improved access to clinical assessments, while better understanding of the somewhat atypical presentation of ASD symptoms in this group may aid clinicians in the diagnostic process. Earlier recognition of ASD in children with DS who have the dual diagnosis could also help to improve educational and behavioural outcomes by facilitating access to broader interventions. However, the finding of an atypical autism profile in this group also suggests the need for the development of specifically targeted interventions.

Summary

Using the largest sample to date, we identified the proportion of children with DS meeting cut-off scores for ASD and autism on the SCQ to be 37.7% and 16.5% respectively. These figures are much higher than those reported in previous studies, probably because of differences in sampling methods and sample characteristics. Children with DS and ASD showed a distinct autism profile compared with an ASD reference group. They were also reported to have higher levels of emotional symptoms, conduct problems, hyperactivity and communication difficulties than individuals with DS only. Reports of regression, in both general and language skills, were higher in children with DS who met the cut-off score for ASD. These findings provide support for previous reports that suggest individuals with DS and ASD have a distinct phenotypic presentation. Further, more detailed, investigation using direct assessment and observational measures is required to gain a better understanding of the difficulties and needs of children with both DS and ASD.

Acknowledgements

We are grateful to the UK Down's Syndrome Association, and particularly to Stuart Mills, for their help with participant recruitment, and to Ellie Walsh and Jennie Cox for their help with the survey distribution, as well as to all the families who participated in the study. This study was funded by a PhD studentship from the Baily Thomas Research Trust.

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Appendix B

1. **Questionnaire survey information sheet and consent form**
2. **Copyright correspondence**
    a) Email from the Social Communication Questionnaire Rights and Permissions Coordinator
    b) Emails from the author of the Strengths and Difficulties Questionnaire
3. **General Information Questionnaire**
4. **Effect size equations**
5. **Ethical approval letter**

B.1

INFORMATION SHEET FOR PARTICIPANTS (Study 1; Postal Survey)

REC Reference Number: PNM/10/11-4

KING'S College LONDON

Title of study: DIFFERENCES AMONG CHILDREN WITH DOWN SYNDROME: A NATIONWIDE SURVEY

Dear Parent,

We would like to invite you to take part in a survey investigating the development of children with Down syndrome. The study is funded by the Baily Thomas Charitable Fund. We have contacted you via the Down Syndrome Association (DSA) and so your personal details are not known to us. You should only participate if you want to; choosing not to take part will not disadvantage you in any way. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

The reasons for the study

Over recent years the prospects for children with Down syndrome and their families have become ever more positive. Many children are now educated in mainstream schools and go on to college and later into work, and many have very active social lives. However, for a small minority the situation is more difficult and some children have severe social, communication and behavioural problems that can make life very difficult for them and their families. In a few cases children with Down syndrome may even have an additional disorder such as autism. We know from members of the DSA that these families can experience many difficulties, and some doctors still hold the view that children with Down syndrome cannot have other disorders. The purpose of this survey is to try to find out what proportion of children with Down syndrome in England and Wales do have additional problems of this kind and what the experience of their families has been in trying to get the help and support they need. By contacting hundreds of families who are members of the DSA this study will give us very valuable information on the typical development of most children with Down syndrome. However, the findings will also tell us about the small minority of children who have additional problems and will be used to alert doctors and other professionals to the fact that some children with Down syndrome do develop differently and have special needs that require specialist help and services.

Who will be involved?

We are asking families in England and Wales who are on the DSA database and who have a child with Down syndrome aged between 6 and 15 years, if they would be willing to take part. The questionnaires have been sent out on our behalf by the DSA - we do not have any access to the information they have on their family members.

Do I have to take part?

Of course that is entirely up to you to decide. This information sheet describes the study and if you wish to take part all you need to do is to complete the enclosed questionnaires. Completing and sending off the questionnaire pack to us will indicate your consent to participate. You are free to withdraw at any time, without giving a reason. So, if later on you decide that you do not want us to use the questionnaires that you have returned then they will be destroyed. This can be done at any stage up to the date of the publication of the study.

What does the study involve?

We are asking you to complete a set of questionnaires about your son or daughter with Down syndrome. These should only take a few minutes each to complete. One of these questionnaires asks about your son's/daughter's social and communication skills, one asks about any behavioural problems your son/daughter may have and the final questionnaire asks for some more general information.

Although the questionnaires provide space for a name, you do *not* need to give your or your child's name or any other identifying details, although we *do* need you to indicate the age and sex of your child, the number of siblings and what area of the country you live in (so we can find out if parents in some parts of the country have more difficulties in getting help than others).

However, later on we will be asking a small number of families if they would be willing to see us for a more detailed assessment of their child. So, your pack also includes a separate form asking if you would be happy for us to contact you again with information about some future research. If you would be willing for us to contact you again then we will need you to give us your contact details so that we can get in touch. You are free to change your mind about this at any time without giving a reason and if you have provided contact details but then decide that you do not want to be contacted then your details will be destroyed. A follow-up study would be subject to further information and consent procedures, and our contacting you again would not imply that you have agreed to take part in future research.

What do I need to do?

Please complete the enclosed questionnaires as fully as you can and return them in the stamped addressed envelope provided. You should not take too long over any of the questions, we just need you to give us a general picture of what your child is like and any particular difficulties he/she may have. If you want to give us any additional information please feel free to do so. Please don't be concerned that many of the questions seem to focus on difficulties rather than your child's skills or achievements. This is because we are trying to find out about children with Down syndrome who need more help than others. If you want to ask any particular questions please do so and we will do our best to respond to these.

What will happen to the information?

The information you provide will be analysed by computer and kept on a confidential database that is only accessible to those working on the project. You do not need to provide us with your name and address but if you choose to do so this information will be kept separately from the questionnaire data and your details will be identifiable only by means of a code throughout the study to ensure anonymity. If published, the findings from the study will be presented without reference to any identifying information. Any personal information that you provide will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998.

What are the possible benefits of taking part?

We cannot promise that the study will be of benefit to you or your family personally but if issues arise about which we can offer advice (e.g. possible sources of help or support) we will do all we can to provide this. The findings will be made available to all families via the DSA website and we hope that the information obtained will be of particular help to children with Down syndrome who have additional problems, such as autism, and in identifying the services their families may need.

What if I have other queries about the project, either now or later?

If you have any questions about the survey please contact Georgina Warner by telephone: 0207 848 5717, or email: georgina.warner@kcl.ac.uk or at the following address: Dept of Psychology, PO77, Henry Wellcome Building, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF

It is up to you to decide whether to take part or not. If you decide to take part you are still free to withdraw at any time and without giving a reason. Your information can be withdrawn at any stage up to the date of the publication of the study.

If this study has harmed you in any way you can contact King's College London using the following details for further advice and information: Professor Patricia Howlin: 020 7848 0815; patricia.howlin@kcl.ac.uk; Dept of Psychology, PO77, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF

Thank you very much for taking the time to read this information. We do hope we have provided you with all the information you need and that you will be able to take part.

CONSENT TO BE CONTACTED ABOUT A FURTHER STUDY ABOUT THE DIFFERENCES AMONG CHILDREN WITH DOWN SYNDROME

KING'S College LONDON

Thank you for completing the anonymous questionnaires about your child.

If you would be willing for us to contact you again about a more detailed study, please provide some contact details below so that we can get in touch. Please complete whichever you would prefer us to contact you on.

A follow-up study would be subject to further information and consent procedures, and our contacting you again would not imply that you have agreed to take part in future research.

Only approved members of our research team would have access to your details. We would not share your details with anyone outside of the research team. You are free to change your mind about us holding your contact details at any time without giving a reason and your information will be destroyed. All you would need to do is contact *Georgina Warner* by telephone, 0207 848 5717, or by email at georgina.warner@kcl.ac.uk or by post at PO77, Henry Wellcome Building, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF.

Title of Study: DIFFERENCES AMONG CHILDREN WITH DOWN SYNDROME

King's College Research Ethics Committee Ref: PNM/10/11-4

Please initial the boxes

- I consent to be contacted again about a more detailed study of differences among children with Down syndrome. ☐
- I understand that my name and contact details will be kept by the research team at King's College, London in accordance with the provisions of the Data Protection Act 1998. ☐
- I understand that even after I have agreed for my details to be kept by the research team at King's College, London, I can request that they be removed, without giving reason, by contacting *Georgina Warner* by telephone, 0207 848 5717, or by email at georgina.warner@kcl.ac.uk or by post at PO77, Henry Wellcome Building, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF. ☐

Name: _____

Please complete whichever you would prefer us to contact you on.

Email: _____

Telephone: _____

Address: _____

_____

King's College London - Research Ethics
2010/2011/1

B.2.a

Following up the licensed use for adapted/on-line application of SCQ material

Angela Ortiz <aortiz@wpspublish.com>

Thu 13/10/2011 00:32

To:Warner, Georgina <georgina.warner@kcl.ac.uk>;

Cc:Fred Dinkins <fdinkins@wpspublish.com>; Susan Weinberg <sweinberg@wpspublish.com>;

Hi Georgina--

With reference to your message below, this email confirms that WPS has vetted your website and we find the following:

SCQ
1) Password protection is appropriate.

2) Placement of the WPS copyright notice is fine.

3) The instructions are appropriately reprinted.

4) The item content is not appropriately numbered. The questions (on page 2) should read #s 20-40 and not #1-21

On provision that you attend/correct the content as indicated in comments 4) you are clear to proceed with your registered application, without any further vet by WPS.

Please let me know if you have any other questions.

Sincerely,

Angela Ortiz
Rights & Permissions Coordinator

Western Psychological Services
625 Alaska Avenue, Torrance, CA 90503-5124

Phone: (424) 201-8800
(800) 648-8857
Fax: (424) 201-6950

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CreativeTherapyStore.com - *Get Creative*™

B.2.b

RE: Permission to use the Strengths & Difficulties Questionnaire

Goodman, Robert <robert.goodman@kcl.ac.uk>

Tue 19/07/2011 16:43

To:Warner, Georgina <georgina.warner@kcl.ac.uk>;

Hi Georgia

Thanks for checking with me. Under the current copyright terms (see bottom of front page of www.sdqinfo.org), it is not permissible for anyone other than Youthinmind to create their own electronic version of the SDQ. However, we at Youthinmind do recognize that there are many advantages to users of computerized administration, including major cost savings on printing, postage and administrative time. It is for this reason that we are now piloting a two-track system:

1) Youthinmind will continue indefinitely to make paper copies of the SDQ available without charge for non-commercial use that does not involve any charge to families – and we are working on increasing the range of language options (primarily by including more African and Asian languages). We will also make free scoring software available for these users.

2) Users who want to use their own electronic versions of the SDQ and benefit from the economies of doing so will need to pay a small license fee (10p per SDQ administered) to Youthinmind, with this income being used to cover Youthinmind's central costs, and thereby ensuring that free paper SDQs stay available indefinitely. The conditions of use of the SDQ will include:

a) Licensees need to keep track of the exact number of SDQs administered, and be able to justify, if requested, the total that they declare.

b) Licensees pay Youthinmind the license fee at regular intervals: quarterly, 6-monthly or yearly at the Licensee's convenience. The fee is strictly per item, with no reduction for large users. (Since we expect users to save money by using the license, larger users are already advantaged by saving larger amounts of money).

c) The web presentation of the SDQ cannot involve any change in wording and needs to be as close as possible to the standard paper version in appearance - no bright colours, flashing icons etc. This is because changes in presentation can undermine the comparability of SDQ data collected in different ways, making it harder to combine or contrast SDQ data from different studies or clinics. The copyright notice on the paper version also needs to be present on the electronic version.

d) The license will be revoked if the SDQ were being used in a way likely to bring it into disrepute.

It is obviously entirely up to you as to whether you would rather use the paper copies free, be included among the "pilot" groups who pay a license fee to create their own legal online version, or switch to some other measure that can be deployed online without charge.

Please let me know if you need further clarification.

Best wishes
Robert

RE: Permission to use the Strengths & Difficulties Questionnaire

Goodman, Robert <robert.goodman@kcl.ac.uk>

Wed 12/10/2011 09:06

To:Warner, Georgina <georgina.warner@kcl.ac.uk>;

Hi Georgina
Thank you for taking so much care in making your online version of the SDQ identical to the paper version. You are now authorized by us to use it in accordance with the license.
Good luck with your study
Robert

B.3

General Information

Please initial the box

I consent to the processing of my personal information for the purposes explained to me. I understand that such information will be handled in accordance with the terms of the Data Protection Act 1998. ☐

1. What method of communication does your child use?

☐ Phrase/Sentence Speech ☐ Gesture

☐ Single Words ☐ None

☐ Signs ☐ Other e.g. Switches, Communication Board (please specify)

☐ Picture Exchange

2. If your child does use speech, at approximately what age did s/he first use words meaningfully, apart from "mama" and "dada"?

☐ months

3. Have you ever been concerned that your child has lost language skills?

☐ Yes ☐ No

4. If "Yes", how old was s/he when this loss first became apparent?

☐ months

5. Have you ever been concerned that your child has lost general skills?

☐ Yes ☐ No

6. If "Yes", how old was s/he when this loss first became apparent?

☐ months

7. Do you feel that your child's education is appropriate for his/her needs?

☐ Yes ☐ No

8. Have you ever sought alternative educational provision?

☐ Yes ☐ No

9. If "Yes", please give details below:

10. What is the genetic source of your child's Down syndrome?

☐ Trisomy 21 ☐ Translocation

☐ Mosaicism ☐ Don't Know

11. Have you ever had the feeling that your child does not fit the "typical" Down syndrome profile?

☐ Yes ☐ No

12. If "Yes", in what way do feel that your child does not fit the "typical" Down syndrome profile?

Please tick all that apply.

☐ Behavioural & Emotional Problems ☐ Motor Skills

☐ Social Communication ☐ Other (please specify)

☐ Play Skills

Please give any details below:

13. Have you ever sought a further diagnosis?

☐ Yes ☐ No

14. If "Yes", please give details below:

15. What town/city do you live in?

This information is to find out if parents in some parts of the country have more difficulties in getting help than others.

16. How many other children are there in the family?

B.4

Effect size equations

$$r = \sqrt{t^2 / (t^2 + df)}$$

Where t = t-test statistic and df = the number of degrees of freedom

$$\text{Cliff's } d = (2U / nm) - 1$$

Where U = Mann Whitney U statistic, n = number of participants in first sample and m = number of participants in second sample

$$\text{Cramer's } V = \sqrt{(\chi^2 / kn)}$$

Where χ^2 = Chi square statistic, k = number of degrees of freedom and n = number of participants

Consequently:

$$\varphi = \sqrt{(\chi^2 / n)}$$

because k=1 and thus becomes redundant.

B.5

Research Ethics Office

5.11 Franklin-Wilkins Building
(Waterloo Bridge Wing)
Stamford Street
London SE1 9NH
Tel 020 7848 4077/4070/4020
Email rec@kcl.ac.uk
www.kcl.ac.uk/research/ethics

KING'S College LONDON

Georgina Warner
Department of Psychology
PO78
Institute of Psychiatry
King's College London
De Crespigny Park
London
SE5 8AF

30 September 2011

Dear Georgina

PNM/10/11-4 The impact on families of having a child with down syndrome and co-morbid autism spectrum disorder (Study 1: Pilot).

Thank you for submitting a modification request for the above study. I am writing to confirm approval of this. The modifications are summarised below:

1. We acknowledge that Georgina Warner has become the lead researcher for the study.
2. The primary research questions for the questionnaire survey have been revised.
3. Measures used in the survey will include the Social and Communication Questionnaire, the Strengths and Difficulties Questionnaire and an additional General Information Questionnaire.
4. The survey will be administered electronically via Select Survey to members of the Down's Syndrome Association that have an email address.
5. The lower age limit for the study has changed from five years of age to six years of age.
6. The survey will only be distributed to those who live in England or Wales.
7. The Information Sheets have been altered to reflect whether the participant is completing the questionnaires online or by post.

If you should have any further queries about your application, please do not hesitate to contact the Research Ethics office.

Yours sincerely

Catherine Fieulleteau
Senior Research Ethics Officer

cc: Patricia Howlin

Appendix C

1. **Group study and impact on the family information sheets and consent forms**
    a) Parent information sheet and consent form
    b) Child information sheet
    c) Head teacher cover letter and consent slip
    d) Teacher information sheet and consent form
2. **Inter-rater reliability subsample characteristics**
3. **Histogram of ADOS-G codes**
4. **Ethical approval letters**
5. **CBQ analyses (need for physical contact / frequency / longest episode)**
6. **Natural observation analyses (group / 1:1 / play)**
7. **Special school vs. mainstream group differences and regression analysis**
8. **Boxplot of Vineland II composite scores by group (DS+ASD / DS-only)**

C.1.a

INFORMATION SHEET FOR CAREGIVERS

KING'S College LONDON

REC Reference Number: PNM/11/12-45

Title of study: DIFFERENCES AMONG CHILDREN WITH DOWN SYNDROME

Dear Parent,

We would like to invite you and your child to take part in a research study investigating the development of children with Down syndrome. The study is funded by the Baily Thomas Charitable Fund. We have contacted you because you have previously agreed for us to keep your personal details and to contact you with information about future research studies conducted by the King's College, London research team. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

The reasons for the study:
Today, many children with Down syndrome are educated in mainstream schools and the majority have very active social lives. However, a small minority has unusually severe social, communication and behavioural problems. Sometimes these children may meet the diagnostic criteria for autism. We know from the Down's Syndrome Association (DSA) that the families of these children can experience many difficulties in accessing appropriate help and support. The purpose of this study is to compare children with Down syndrome who show a very typical "Down syndrome" pattern of development with those children with Down syndrome who show more severe social and communication difficulties. The findings of this study will tell us about patterns of development in this exceptional group of children and the impact on families. Our aim is to improve understanding of the needs of these children and to alert professionals to the help their families from medical, social and educational services.

Why have I been invited?
Some time ago you completed a survey about the development of children with Down syndrome and we are now asking some of the families who took part then if they would be willing to take part in a more detailed assessment of their children's functioning. You very kindly gave us your contact details in order that we might contact you again and that is the reason we are writing to you now.

Do I have to take part?
Of course that is entirely up to you. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You are free to withdraw at any time, without giving a reason. You may withdraw your data up to the point of publication. This would not affect the care that you or any member of your family is receiving. Choosing not to take part will not disadvantage you in any way.

What will happen if I take part?
First we will ask you to complete some questionnaires about your child's development and any specific problems he/she may have. These can be completed whenever you wish and will probably take around 1 hour 30 minutes. Then we would like to conduct a telephone interview with you to discuss your child's cognitive abilities. This will probably take about 45 minutes. Finally we would like to visit your child at school to provide his/her teacher with a questionnaire about behavioural and emotional problems and conduct an assessment of your child's social, communication and play skills using a play based observation. This involves observing how your child interacts with different toys and activities and also with the interviewer. We would like to video record this assessment so that other members of our research team can rate how well your child has responded. This part of the assessment will probably take around 2 hours in total.

The assessments of your child will usually take place at school, but can also be arranged at home, depending on what is most convenient for you. All visits will be arranged at a time that best suits you and your child. If the assessments highlight any particular areas of difficulty with which you would like more help (e.g. behaviour management; seeking specialist medical or clinical

assessment) we will advise how you might go about seeking this and/or help to facilitate a referral to relevant services. After the assessments are complete you will receive a written summary of the findings.

How will video recordings be made?
Video recordings will only take place during previously specified times that have been agreed by teachers and parents/carers. Your child's privacy and dignity will be respected and video recordings will not take place if there is any indication that the observations are causing distress. You may keep a copy of the video if you wish. When videotapes are not in use they will be stored in a locked cabinet in the Institute of Psychiatry, King's College, London and will only be viewed by researchers involved in the study. Information identifying your child will not be stored on or with the tape. Any data that are derived from the tape will remain anonymous. Video recordings will not be shown for the purpose of teaching.

What are the possible benefits of taking part?
Many families find the personal feedback report useful; however, we cannot promise that the study will be of benefit to you or your family personally. If issues arise about which we can offer help or advice we will do all we can to provide this.

What are the possible disadvantages of taking part?
The study will take up a few hours of your time, although many the questionnaires can be completed as and when you have time and do not all have to be done in one go. The play activities involved in the assessment of your child have been developed especially for children with special needs and are usually very much enjoyed by the children. We would offer the opportunity for your child's teacher or yourself to be present when this assessment takes place in order to re-assure your child if this is required. If at any time your child were to become distressed the assessment would stop immediately.

Because of the nature of the study, we will be focussing on areas of difficulty, either for you or your child. Sometimes this can be upsetting for parents, but whenever possible, we will try to advise how you might go about getting more help for any problems you are experiencing (either personal or with regard to the child's education or management etc).

If the study identifies children who are showing significantly greater impairments in social communication skills than would be typical of most children with Down syndrome of that age, we will advise families how to seek a referral for a more detailed assessment. The study will not be able to make clinical diagnoses (e.g. of autism or any other disorder) on the children involved. However, all families will be provided with written information of their scores on the measures completed which will be helpful in further consultations.

What will happen to the information?
All information will be kept on a confidential database that is only accessible to those working on the project. All personal information (names addresses etc) will be kept separate from the main data base and data anonymised so that participants will be identified only by a code number, not by name. Paper files will be kept in locked files at the Institute of Psychiatry and computerised data will be protected by using encrypted and password protected computers, memory sticks and data files. If published, the findings from the study will be presented without reference to any identifying information. Any personal Information that you provide will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998. However, if a disclosure is made to the research team indicating that a child is at significant risk of abuse the appropriate authorities would be informed.

What will happen when the research stops?
We expect the study will take 2 years to complete but we will inform families of on-going progress via the Down's Syndrome Association Website. At the end of the project the findings will be publicised by the Down's Syndrome Association and published in relevant academic journals and presented at relevant conferences. No individuals will be identified at any stage.

What will happen to the results of the study?
A 6 monthly newsletter will be distributed via the Down's Syndrome Association website to inform families of the progress of the study. A summary of the findings, and the implications of these for support services, will be publicised by the Down's Syndrome Association and the National Autistic Society and Research Autism. The final results of the study will be published in relevant academic journals.

What if there is a problem?
If the study has harmed you in any way, or if you have any complaint or concerns about any aspect of the study, you can contact Professor Howlin or Georgina Warner directly by email or phone (patricia.howlin@iop.kcl.ac.uk; tel 020 7848 0243; georgina.warner@kcl.ac.uk tel 020 7848 5717 and we will do our best to answer your questions.

What if I have other queries about the project, either now or later?
If you are unclear about any aspect of the study or have any questions, please contact Georgina Warner by email (Georgina.warner@kcl.ac.uk), telephone (020 7848 5717) or by post at Department of Psychology, P077, Henry Wellcome Building, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF.

Thank you very much for taking the time to read this information. We do hope we have provided you with all the information you need and that you will be able to take part.

CONSENT FORM FOR PARTICIPANTS IN RESEARCH STUDIES

KING'S College LONDON

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: DIFFERENCES AMONG CHILDREN WITH DOWN SYNDROME

King's College Research Ethics Committee Ref: PNM/11/12-45

- **Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.**
- **The results of the study will be published and you will be sent a written summary of the findings. Confidentiality and anonymity will be maintained and it will not be possible to identify you from any publications.**

Please tick or initial

- I understand that if I decide at any time during the research that I no longer wish to participate in this project, I can notify the researchers involved and withdraw from it immediately without giving any reason. Furthermore, I understand that I will be able to withdraw my data up to the point of publication. ☐
- I understand that as part of the above study, video/voice recordings of my child and myself/child's teacher will be made and stored securely stored at the Department of Psychology, King's College. London, for further review by researchers involved in the study. ☐
- I consent to my child's school being contacted to take part in the study and being provided with feedback from the assessments. ☐

  If 'yes', please provide the school contact details below:

  Name of School: _____
  Head Teacher: _____
  Address: _____
  _____
  Telephone: _____

- I consent to the processing of my personal information for the purposes explained to me. I understand that such information will be handled in accordance with the terms of the Data Protection Act 1998. ☐
- I agree to be contacted in the future by King's College, London researchers who would like to invite me to participate in follow up studies to this project, or in future studies of a similar nature. ☐

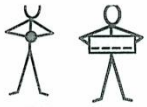
Participant's Statement:

I _____ agree that the research project named above has been explained to me to my satisfaction and I agree to take part in the study. I have read both the notes written above and the Information Sheet about the project, and understand what the research study involves.

Signed **Date**

King's College London - Research Ethics
2010/2011/1

C.1.b

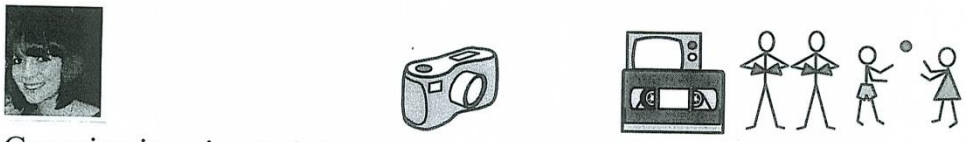


My name is _____

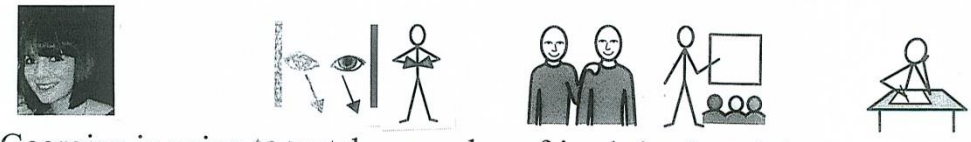
A lady called Georgina is going to visit me at school.

Georgina is going to play games with me.

Georgina is nice and we will have fun.



Georgina is going to bring a camera to make a video of us playing.



Then Georgina is going to watch me and my friends in class doing our work.

Georgina will tell _____ all about our day.

This study has been approved by the Psychiatry, Nursing and Midwifery Research Ethics Subcommittee, King's College London (Reference Number PNM/11/12-45)

C.1.c

[Name of Head Teacher]
[School Address]

Georgina Warner
Department of Psychology
Institute of Psychiatry
King's College London
De Crespigny Park
London
SE5 8AF

020 7848 5717

georgina.warner@kcl.ac.uk

[Date]

Dear [Name of Head Teacher]

Involvement in Research Project (Ref. PNM/11/12-45)

The caregiver of [Name of Child] has given consent to contact you regarding a research project they have chosen to be involved in. The research study is investigating the development of children with Down syndrome. It is being conducted by King's College London in collaboration with the Down's Syndrome Association and is funded by the Baily Thomas Charitable Fund.

If possible we would like to visit [Name of Child] at school to observe him/her for a short time in the classroom and also to carry out a standardised assessment of his/her play, communication and social skills. This assessment would be done in a separate room and would be video recorded so that other members of our research team can rate how well [Name of Child] has responded. All members of the team have enhanced CRB clearance. We would also be very grateful if [Name of Child]'s class teacher could complete a questionnaire about any behavioural and emotional problems that he/she experiences in school. We would need all three of these components for your school to take part in the study.

You will be provided with feedback from the assessment, which may prove beneficial to staff members who work with [Name of Child].

We would only need to visit the school for one day sometime in the next couple of months, at your convenience. Please read the enclosed information sheet for more detail on the research study and, if you are happy to take part and are happy with the CRB clearance of the visiting researcher, please return the attached slip and pass the information sheet and consent form onto [Name of Child]'s class teacher.

On receipt of both permission by yourself and consent from the class teacher I will contact you again to arrange a date for the visit.

Please do not hesitate to contact me if you have any questions about the study.

Yours Sincerely,

Georgina Warner

I give permission for the Differences among Children with Down Syndrome research project (Ref. PNM/11/12-45) to take place in my school. ☐

Presentation of an enhanced CRB disclosure form for King's College London will be satisfactory for the visit. *Please Note. A school staff member may be present at all times during the assessments.* ☐

Name of Head Teacher _____

Name of School _____

Signed _____ Date _____

C.1.d

INFORMATION SHEET FOR TEACHERS

KING'S College LONDON

REC Reference Number: PNM/11/12-45

Title of study: DIFFERENCES AMONG CHILDREN WITH DOWN SYNDROME

Dear Teacher,

We would like to invite you to take part in a research study investigating the development of children with Down syndrome. The study is funded by the Baily Thomas Charitable Fund. We have contacted you because you teach one of the children involved in the study. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

The reasons for the study:
Today, many children with Down syndrome are educated in mainstream schools and the majority have very active social lives. However, a small minority has unusually severe social, communication and behavioural problems. Sometimes these children may meet the diagnostic criteria for autism. We know from the Down's Syndrome Association (DSA) that the families of these children can experience many difficulties in accessing appropriate help and support. The purpose of this study is to compare children with Down syndrome who show a very typical "Down syndrome" pattern of development with those children with Down syndrome who show more severe social and communication difficulties. The findings of this study will tell us about patterns of development in this exceptional group of children and the impact on families. Our aim is to improve understanding of the needs of these children and to alert professionals to the help their families from medical, social and educational services.

Why have I been invited?
The caregiver of a child you teach has given us permission to contact you to see if you would like to take part in the study and give the school's perspective on the development of the child. The Head Teacher of your school has given permission for the study to take place in your school.

Do I have to take part?
Of course that is entirely up to you. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You are free to withdraw at any time, without giving a reason. You may withdraw your data up to the point of publication. Choosing not to take part will not disadvantage you in any way.

What will happen if I take part?
We will visit you and the child at the school. First we will ask you to complete a questionnaire about any behavioural and emotional problems the child displays. Then we will conduct an assessment of the child's social, communication and play skills using a play based observation. This involves observing how the child interacts with different toys and activities and also with the interviewer. We would like to video record this assessment so that other members of our research team can rate how well the child has responded. After this we would like to observe the child for a short time in the classroom. After the assessments are complete you will receive a written summary of the findings. We would need to complete *all three* of these activities if you do agree to take part in the study.

How will video recordings be made?
Video recordings will only take place during previously specified times that have been agreed by you and the Head Teacher. The child's privacy and dignity will be respected and video recordings will not take place if there is any indication that the observations are causing distress. When videotapes are not in use they will be stored in a locked cabinet in the Institute of Psychiatry, King's College, London and will only be viewed by researchers involved in the study. Information

identifying the child will not be stored on or with the tape. Any data that are derived from the tape will remain anonymous. Video recordings will not be shown for the purpose of teaching.

What are the possible benefits of taking part?
Many schools find the feedback report useful; however, we cannot promise that the study will be of benefit to you personally. If issues arise about which we can offer help or advice we will do all we can to provide this.

What are the possible disadvantages of taking part?
The assessment will take up a few hours of the child's school time, and the questionnaire a few minutes of your time. The play activities involved in the assessment of the child have been developed especially for children with special needs and are usually very much enjoyed by the children. We would offer the opportunity for you or another member of staff who knows the child well to be present when this assessment takes place in order to reassure the child if this is required. If at any time the child were to become distressed the assessment would stop immediately.

What will happen to the information?
All information will be kept on a confidential database that is only accessible to those working on the project. All personal information (names addresses etc) will be kept separate from the main data base and data anonymised so that participants will be identified only by a code number, not by name. Paper files will be kept in locked files at the Institute of Psychiatry and computerised data will be protected by using encrypted and password protected computers, memory sticks and data files. If published, the findings from the study will be presented without reference to any identifying information. Any personal information that you provide will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998. However, if a disclosure is made to the research team indicating that a child is at significant risk of abuse the appropriate authorities would be informed.

What will happen when the research stops?
We expect the study will take 2 years to complete. At the end of the project the findings will be publicised by the Down's Syndrome Association and published in relevant academic journals and presented at relevant conferences. No individuals will be identified at any stage.

What will happen to the results of the study?
A summary of the findings, and the implications of these for support services, will be publicised by the Down's Syndrome Association and the National Autistic Society and Research Autism. The final results of the study will be published in relevant academic journals.

What if there is a problem?
If the study has harmed you in any way, or if you have any complaint or concerns about any aspect of the study, you can contact Professor Howlin or Georgina Warner directly by email or phone (patricia.howlin@iop.kcl.ac.uk; tel 020 7848 0243; georgina.warner@kcl.ac.uk tel 020 7848 5717) and we will do our best to answer your questions.

What if I have other queries about the project, either now or later?
If you are unclear about any aspect of the study or have any questions, please contact Georgina Warner by email (Georgina.warner@kcl.ac.uk), telephone (020 7848 5717) or by post at Department of Psychology, P077, Henry Wellcome Building, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF.

Thank you very much for taking the time to read this information. We do hope we have provided you with all the information you need and that you will be able to take part.

CONSENT FORM FOR PARTICIPANTS IN RESEARCH STUDIES

KING'S College LONDON

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: DIFFERENCES AMONG CHILDREN WITH DOWN SYNDROME

King's College Research Ethics Committee Ref: PNM/11/12-45

- **Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.**
- **The results of the study will be published and you will be sent a written summary of the findings. Confidentiality and anonymity will be maintained and it will not be possible to identify you from any publications.**

Please tick or initial the appropriate boxes

- I understand that if I decide at any time during the research that I no longer wish to participate in this project, I can notify the researchers involved and withdraw from it immediately without giving any reason. Furthermore, I understand that I will be able to withdraw my data up to the point of publication. ☐
- I understand that as part of the above study, video/voice recordings of school staff members and the named child will be made and stored securely stored at the Department of Psychology, King's College. London, for further review by researchers involved in the study. ☐
- I consent to the processing of my personal information for the purposes explained to me. I understand that such information will be handled in accordance with the terms of the Data Protection Act 1998. ☐
- I agree to be contacted in the future by King's College, London researchers who would like to invite me to participate in follow up studies to this project, or in future studies of a similar nature. ☐

Participant's Statement (*Class Teacher*):

I _____ agree that the research project named above has been explained to me to my satisfaction and I agree to take part in the study. I have read both the notes written above and the Information Sheet about the project, and understand what the research study involves.

Signed **Date**

King's College London - Research Ethics
2010/2011/1

C.2

Inter-rater reliability subsample characteristics

ADOS-G Co-rater: Dr Erica Salomone, Institute of Psychiatry

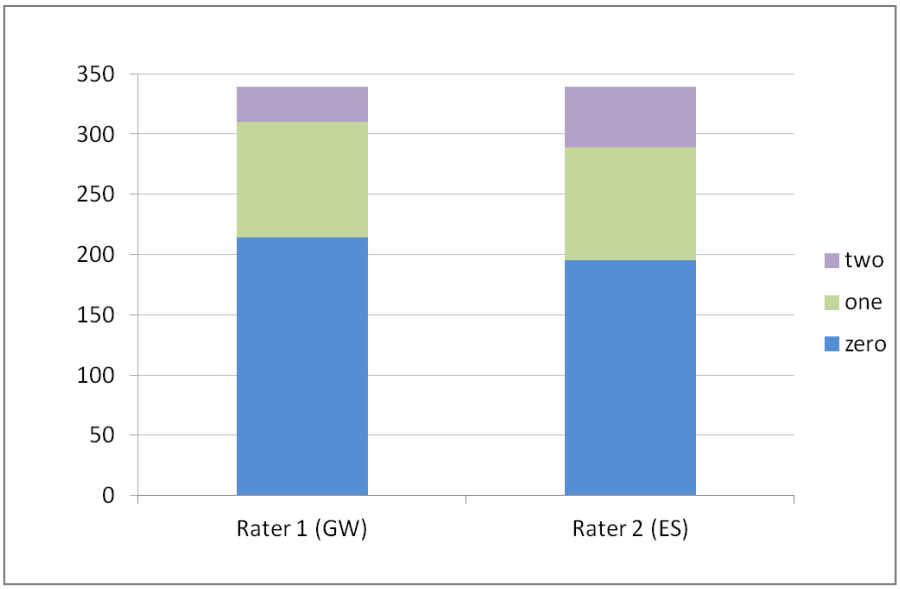
Username	Gender	Age (Years)	Module
C1	Female	10	2
C6	Male	15	1
C7	Male	9	1
C17	Male	14	2
C21	Male	13	1
C22	Female	9	2
C38	Male	12	3
C41	Female	9	3
C42	Male	14	3
C48	Male	11	3
C50	Female	11	3
C51	Male	11	3
	% male = 66.7	Mean age = 11.5	

Natural Observation (Obswin) Co-rater: Miss Kellyan Gayle, Institute of Psychiatry

Username	Gender	Age (Years)
C1	Female	10
C3	Female	16
C5	Male	15
C6 (live coding)	Male	15
C7	Male	9
C17	Male	14
C20	Male	8
C39	Female	16
C40	Male	13
C42	Male	14
C48	Male	11
	% male = 72.7	Mean age =12.8

C.3

Histogram of ADOS-G codes



C.4.a

Research Ethics Office

5.11 Franklin-Wilkins Building
(Waterloo Bridge Wing)
Stamford Street
London SE1 9NH
Tel 020 7848 4077/4070/4020
Email rec@kcl.ac.uk
www.kcl.ac.uk/research/ethics

KING'S College LONDON

Georgina Warner
PO78 Department of Psychology
Institute of Psychiatry
De Crespigny Park
SE5 8AF

08 February 2012

Dear Georgina

PNM/11/12-45 Down Syndrome and Co-Morbid Autism: A Comparative Study.

Review Outcome: Full Approval

Thank you for sending in the amendments/clarifications requested to the above project. I am pleased to inform you that these meet the requirements of the PNM RESC and therefore that full approval is now granted with the following proviso:

1. Section 2.8: Once obtained, please provide copies of written evidence from the schools involved in the study confirming that they are satisfied with your enhanced CRB clearance for King's College London to the Research Ethics Office.

Please ensure that you follow all relevant guidance as laid out in the King's College London Guidelines on Good Practice in Academic Research (http://www.kcl.ac.uk/college/policyzone/index.php?id=247).

For your information ethical approval is granted until **08 February 2015**. If you need approval beyond this point you will need to apply for an extension to approval at least two weeks prior to this explaining why the extension is needed, (please note however that a full re-application will not be necessary unless the protocol has changed). You should also note that if your approval is for one year, you will not be sent a reminder when it is due to lapse.

Ethical approval is required to cover the duration of the research study, up to the conclusion of the research. The conclusion of the research is defined as the final date or event detailed in the study description section of your approved application form (usually the end of data collection when all work with human participants will have been completed), not the completion of data analysis or publication of the results. For projects that only involve the further analysis of pre-existing data, approval must cover any period during which the researcher will be accessing or evaluating individual sensitive and/or un-anonymised records. Note that after the point at which ethical approval for your study is no longer required due to the study being complete (as per the above definitions), you will still need to ensure all research data/records management and storage procedures agreed to as part of your application are adhered to and carried out accordingly.

If you do not start the project within three months of this letter please contact the Research Ethics Office.

Should you wish to make a modification to the project or request an extension to approval you will need approval for this and should follow the guidance relating to modifying approved applications: http://www.kcl.ac.uk/innovation/research/support/ethics/applications/modifications.aspx
The circumstances where modification requests are required include the addition/removal of participant groups, additions/removal/changes to research methods, asking for additional data from participants, extensions to the ethical approval period. Any proposed modifications should only be carried out once

full approval for the modification request has been granted.

Any unforeseen ethical problems arising during the course of the project should be reported to the approving committee/panel. In the event of an untoward event or an adverse reaction a full report must be made to the Chair of the approving committee/review panel within one week of the incident.

Please would you also note that we may, for the purposes of audit, contact you from time to time to ascertain the status of your research.

If you have any query about any aspect of this ethical approval, please contact your panel/committee administrator in the first instance (http://www.kcl.ac.uk/innovation/research/support/ethics/contact.aspx). We wish you every success with this work.

With best wishes

Yours sincerely

Catherine Fieulleteau
Senior Research Ethics Officer

cc: Professor Patricia Howlin

C.4.b

Research Ethics Office

5.11 Franklin-Wilkins Building
(Waterloo Bridge Wing)
Stamford Street
London SE1 9NH
Tel 020 7848 4077/4070/4020
Email rec@kcl.ac.uk
www.kcl.ac.uk/research/ethics

KING'S College LONDON

Georgina Warner
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Dear Georgina

PNM/11/12-45 Down Syndrome and Co-Morbid Autism: A Comparative Study.

Thank you for submitting a modification request for the above study. I am writing to confirm approval of this and the modification is summarised below:

1. A new instrument will be added to the study: Pervasive Development Disorder in Mental Retardation Scale, PDD-MRS.

If you have any questions regarding this application please contact the Research Ethics Office.

Yours sincerely

Catherine Fieulleteau
Senior Research Ethics Officer

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C.5

CBQ analyses (need for physical contact / frequency / longest episode)

SPSS output

Self Injurious behaviour = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of LongestSIB is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.	Unable to compute.
2	The distribution of SIBPrevention is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.	Unable to compute.
3	The distribution of SIBHowOften is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.	Unable to compute.

Physical aggression = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of LongestPA is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.878[1]	Retain the null hypothesis.
2	The distribution of PAPrevention is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	1.000[1]	Retain the null hypothesis.
3	The distribution of PAHowOften is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.412[1]	Retain the null hypothesis.

Destruction of property = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of LongestDOP is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.020[1]	Reject the null hypothesis.
2	The distribution of DOPPrevention the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.133[1]	Retain the null hypothesis.
3	The distribution of DOPHowOften is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.058[1]	Retain the null hypothesis.

Stereotyped behaviour = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of LongestSB is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.330[1]	Retain the null hypothesis.
2	The distribution of SBPrevention is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.402[1]	Retain the null hypothesis.
3	The distribution of SBHowOften is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.145[1]	Retain the null hypothesis.

Refusal to comply = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of LongestRTC is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.180	Retain the null hypothesis.
2	The distribution of RTCPrevention is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.001	Reject the null hypothesis.
3	The distribution of RTCHowOften is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.020	Reject the null hypothesis.

C.6

Natural observation analyses (group / 1:1 / play)

SPSS output

Aggression = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of AGGGroup is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.336[1]	Retain the null hypothesis.
2	The distribution of AGG1to1 is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.114[1]	Retain the null hypothesis.
3	The distribution of AGGPlay is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.267[1]	Retain the null hypothesis.

Destruction of property = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of DSTGroup is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.128[1]	Retain the null hypothesis.
2	The distribution of DST1to1 is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.786[1]	Retain the null hypothesis.
3	The distribution of DSTPlay is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.413[1]	Retain the null hypothesis.

Stereotyped behaviour = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of STBGroup is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.167[1]	Retain the null hypothesis.
2	The distribution of STB1to1 is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.232[1]	Retain the null hypothesis.
3	The distribution of STBPlay is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.000[1]	Reject the null hypothesis.

Refusal to comply = Yes

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of RTCGroup is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.608[1]	Retain the null hypothesis.
2	The distribution of RTC1to1 is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.282[1]	Retain the null hypothesis.
3	The distribution of RTCPlay is the same across categories of GroupADOSonly.	Independent-Samples Mann-Whitney U Test	.743[1]	Retain the null hypothesis.

C.7

Special school vs. mainstream school group differences and regression analysis SPSS outputs

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Vineland II Composite is the same across categories of SchoolMvsS.	Independent-Samples Mann-Whitney U Test	.000	Reject the null hypothesis.
2	The distribution of TotalDBCT is the same across categories of SchoolMvsS.	Independent-Samples Mann-Whitney U Test	.017	Reject the null hypothesis.
3	The distribution of ADOS CSS is the same across categories of SchoolMvsS.	Independent-Samples Mann-Whitney U Test	.000	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Model summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	.758[a]	.574	.562	.335	.574	47.244	1	35	.000

a. Predictors: (Constant), Vineland II Composite

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	2.134	.242		8.814	.000
	Vineland II Composite	-.028	.004	-.758	-6.873	.000

a. Dependent Variable: SchoolMvsS

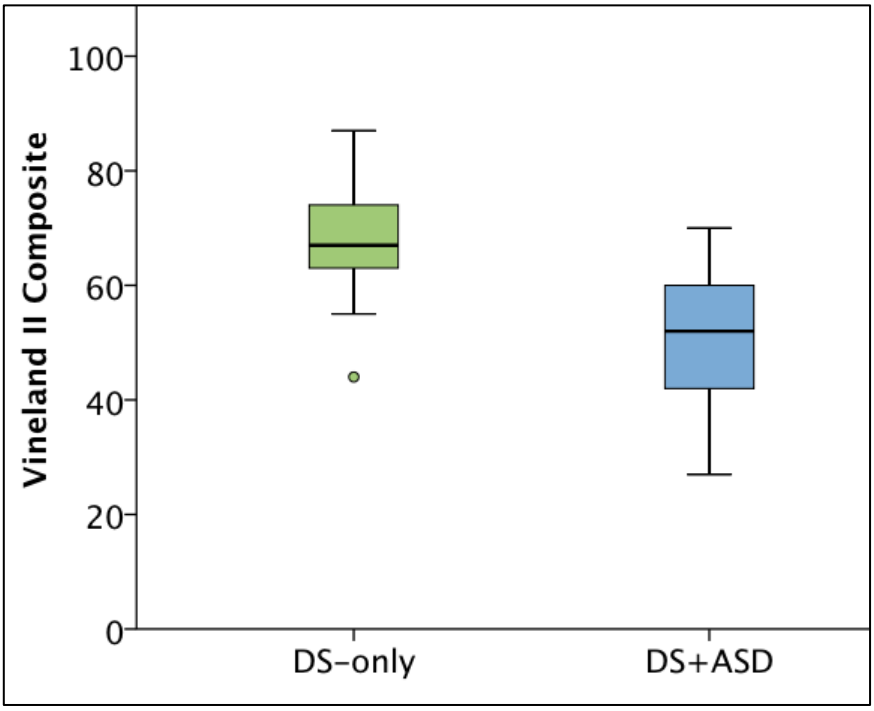
Excluded Variables[a]

Model		Beta In	t	Sig.	Partial Correlation	Collinearity Statistics
						Tolerance
1	TotalDBCT	.001[b]	.010	.992	.002	.673
	ADOS CSS	.254[b]	1.847	.073	.302	.602

a. Dependent Variable: SchoolMvsS
b. Predictors in the Model: (Constant), Vineland II Composite

C.8

Boxplot of Vineland II composite scores by group (DS+ASD / DS-only)



Appendix D

ADOS-G training certificate

Institute of Psychiatry

at The Maudsley

Professor Patrick Bolton
Professor of Child & Adolescent Psychiatry

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K LONDON
Founded 1829

University of London

THIS IS TO CERTIFY THAT

Georgina Warner

HAS ATTENDED

A TRAINING COURSE IN THE

ADMINISTRATION OF THE AUTISM DIAGNOSTIC

OBSERVATION SCHEDULE – GENERIC

Patrick Bolton

PROF. PATRICK BOLTON

DATE 20/07/2011